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DATE: Monday, March 08, 2004 Printable Copy Create Case

Set Name side by side	Query	Hit Count	Set Name result set
DB=USPT; PLUR=YES; OP=OR			
L6	l4 and angiogenesis	0	L6
L5	l3 and L4	0	L5
L4	McCrae.in.	52	L4
L3	angiogenesis adj inhibit	43	L3
L2	kininogen adj2 angiogenesis	0	L2
L1	6284726.pn.	1	L1

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 NEWS  2           "Ask CAS" for self-help around the clock
 NEWS  3  SEP 09   CA/CAplus records now contain indexing from 1907 to the
                   present
 NEWS  4  DEC 08   INPADOC: Legal Status data reloaded
 NEWS  5  SEP 29   DISSABS now available on STN
 NEWS  6  OCT 10   PCTFULL: Two new display fields added
 NEWS  7  OCT 21   BIOSIS file reloaded and enhanced
 NEWS  8  OCT 28   BIOSIS file segment of TOXCENTER reloaded and enhanced
 NEWS  9  NOV 24   MSDS-CCOHS file reloaded
 NEWS 10  DEC 08   CABA reloaded with left truncation
 NEWS 11  DEC 08   IMS file names changed
 NEWS 12  DEC 09   Experimental property data collected by CAS now available
                   in REGISTRY
 NEWS 13  DEC 09   STN Entry Date available for display in REGISTRY and CA/CAplus
 NEWS 14  DEC 17   DGENE: Two new display fields added
 NEWS 15  DEC 18   BIOTECHNO no longer updated
 NEWS 16  DEC 19   CROPU no longer updated; subscriber discount no longer
                   available
 NEWS 17  DEC 22   Additional INPI reactions and pre-1907 documents added to CAS
                   databases
 NEWS 18  DEC 22   IFIPAT/IFIUDB/IFICDB reloaded with new data and search fields
 NEWS 19  DEC 22   ABI-INFORM now available on STN
 NEWS 20  JAN 27   Source of Registration (SR) information in REGISTRY updated
                   and searchable
 NEWS 21  JAN 27   A new search aid, the Company Name Thesaurus, available in
                   CA/CAplus
 NEWS 22  FEB 05   German (DE) application and patent publication number format
                   changes
 NEWS 23  MAR 03   MEDLINE and LMEDLINE reloaded
 NEWS 24  MAR 03   MEDLINE file segment of TOXCENTER reloaded
 NEWS 25  MAR 03   FRANCEPAT now available on STN

 NEWS EXPRESS  MARCH 5 CURRENT WINDOWS VERSION IS V7.00A, CURRENT
               MACINTOSH VERSION IS V6.0b(ENG) AND V6.0Jb(JP),
               AND CURRENT DISCOVER FILE IS DATED 3 MARCH 2004
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=> s angiogenesis
L1      182982 ANGIOGENESIS

=> s l1 and inhibit?
L2       87878 L1 AND INHIBIT?

=> s (cytokine driven inhibition) and angiogenesis
L3           0 (CYTOKINE DRIVEN INHIBITION) AND ANGIOGENESIS

=> s l2 and cytokine
L4       16803 L2 AND CYTOKINE

=> s l4 and carbobenzybxy group
L5           0 L4 AND CARBOBENZYBXY GROUP

=> s t-butyloxycarbonyl
L6        6215 T-BUTYLOXYCARBONYL

=> s l6 and l4
L7         126 L6 AND L4

=> s HK
L8        7254 HK

=> s HKa
L9         241 HKA

=> s l8 and l9
L10         64 L8 AND L9

=> s l10 and l7
L11          0 L10 AND L7

=> d l7 ti abs ibib 1-25
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L7 ANSWER 1 OF 126 USPATFULL on STN
TI Alpha v integrin receptor antagonists
AB The present invention relates to novel chain-fluorinated alkanoic acid derivatives thereof, their synthesis, and their use as αv integrin receptor antagonists. More particularly, the compounds of the present invention are antagonists of the integrin receptors αvβ3 and/or αvβ5 and are useful for **inhibiting** bone resorption, treating and preventing osteoporosis, and **inhibiting** vascular restenosis, diabetic retinopathy, macular degeneration, **angiogenesis**, atherosclerosis, inflammation, inflammatory arthritis, viral disease, cancer, and metastatic tumor growth.

ACCESSION NUMBER: 2004:51532 USPATFULL
TITLE: Alpha v integrin receptor antagonists
INVENTOR(S): Wang, Jiabing, Chalfont, PA, UNITED STATES

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004038963	A1	20040226	
APPLICATION INFO.:	US 2002-276048	A1	20021112	(10)
	WO 2001-US22938		20010720	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
NUMBER OF CLAIMS: 21
EXEMPLARY CLAIM: 1
LINE COUNT: 2712

L7 ANSWER 2 OF 126 USPATFULL on STN
TI Rhamm peptide conjugates
AB The present invention provides protein conjugates having a glucose-aminoglycan-targeting domain conjugated directly or indirectly to a therapeutically useful protein via chemical or peptidyl linkage. The protein conjugates selectively target certain tissues and organs and are useful for treating or preventing various physiological and pathological conditions. Methods of their use and preparation are described.

ACCESSION NUMBER: 2004:50407 USPATFULL
TITLE: Rhamm peptide conjugates
INVENTOR(S): Woloski, B. Michael R., Charlottesville, VA, UNITED STATES
Williams, Ashley Martin, Winnipe Manitoba Canada, CANADA
Sereda, Terrance Jimmy, Winnipeg Manitoba Canada, CANADA
Wiebe, Deanna June, Winnipeg Manitoba Canada, CANADA

	NUMBER	KIND	DATE	
PATENT INFORMATION:	US 2004037834	A1	20040226	
APPLICATION INFO.:	US 2003-257377	A1	20030610	(10)
	WO 2001-CA533		20010420	

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: KNOBLE & YOSHIDA, EIGHT PENN CENTER, SUITE 1350, 1628 JOHN F KENNEDY BLVD, PHILADELPHIA, PA, 19103
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 3766

L7 ANSWER 3 OF 126 USPATFULL on STN
TI Anti-invasive and anti-angiogenic compositions
AB A peptide compound having the sequence Lys-Pro-Ser-Ser-Pro-Pro-Glu-Glu

[SEQ ID NO:2] or a substitution variant, addition variant or other chemical derivative thereof **inhibits** cell invasion, endothelial tube formation or **angiogenesis** in vitro. A number of substitution variants and addition variants of this peptide, preferably capped at the N- and C-termini, as well as peptidomimetic derivatives, are useful for treating diseases and conditions mediated by undesired and uncontrolled cell invasion and/or **angiogenesis**. Pharmaceutical compositions comprising the above peptides and derivatives are administered to subjects in need of such treatment in a dosage sufficient to **inhibit** invasion and/or **angiogenesis** . The disclosed compositions and methods are particularly useful for suppressing the growth and metastasis of tumors.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2004:46789 USPATFULL
TITLE:	Anti-invasive and anti-angiogenic compositions
INVENTOR(S):	Mazar, Andrew P., Escondido, CA, United States Jones, Terence R., San Diego, CA, United States
PATENT ASSIGNEE(S):	Angstrom Pharmaceuticals, Inc., San Diego, CA, United States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6696416	B1	20040224
APPLICATION INFO.:	US 1999-437136		19991110 (9)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 1997-900327, filed on 25 Jul 1997, now patented, Pat. No. US 5994309
DOCUMENT TYPE:	Utility
FILE SEGMENT:	GRANTED
PRIMARY EXAMINER:	Bansal, Geetha P.
LEGAL REPRESENTATIVE:	Livnat, Shmuel, Venable, Baetjer, Howard & Civiletti, LLP
NUMBER OF CLAIMS:	8
EXEMPLARY CLAIM:	1,5
NUMBER OF DRAWINGS:	28 Drawing Figure(s); 24 Drawing Page(s)
LINE COUNT:	2576

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 4 OF 126 USPATFULL on STN

TI Enhanced affinity hyaluronan binding peptides

AB Novel hyaluronan-binding peptides are provided. The peptides are useful in preventing and treating disorders associated with altered tissue levels of hyaluronan or RHAMM, including cancer, inflammatory and autoimmune disorders and fibrotic disorders associated with tissue trauma.

ACCESSION NUMBER:	2004:45207 USPATFULL
TITLE:	Enhanced affinity hyaluronan binding peptides
INVENTOR(S):	Turley, Eva, Toronto, CANADA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004034201	A1	20040219
APPLICATION INFO.:	US 2001-883375	A1	20010619 (9)

RELATED APPLN. INFO.:	Division of Ser. No. US 1998-210896, filed on 16 Dec 1998, GRANTED, Pat. No. US 6271344

	NUMBER	DATE
PRIORITY INFORMATION:	US 1997-68285P	19971219 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Micheline Gravelle, Bereskin & Parr, Box 401, 40 King Street West, Toronto, ON, M5H 3Y2

NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 28 Drawing Page(s)
LINE COUNT: 1915

L7 ANSWER 5 OF 126 USPATFULL on STN
TI Modified mature insulin variants and composition containing same
AB IGF-I and insulin variants are provided that selectively bind to IGFBP-1 or IGFBP-3. These agonist variants are useful, for example, to improve the half-lives of IGF-I and insulin, respectively.

ACCESSION NUMBER: 2004:44959 USPATFULL
TITLE: Modified mature insulin variants and composition containing same
INVENTOR(S): Dubaquie, Yves, San Francisco, CA, UNITED STATES
Lowman, Henry, El Granada, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004033952	A1	20040219
APPLICATION INFO.:	US 2003-444701	A1	20030522 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-724198, filed on 28 Nov 2000, ABANDONED Division of Ser. No. US 2000-477923, filed on 5 Jan 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115010P	19990106 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 275 MIDDLEFIELD ROAD, MENLO PARK, CA, 94025-3506
NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2420

L7 ANSWER 6 OF 126 USPATFULL on STN
TI Modified mature insulin variants and composition containing same
AB IGF-I and insulin variants are provided that selectively bind to IGFBP-1 or IGFBP-3. These agonist variants are useful, for example, to improve the half-lives of IGF-I and insulin, respectively.

ACCESSION NUMBER: 2004:44958 USPATFULL
TITLE: Modified mature insulin variants and composition containing same
INVENTOR(S): Dubaquie, Yves, San Francisco, CA, UNITED STATES
Lowman, Henry, El Granada, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004033951	A1	20040219
APPLICATION INFO.:	US 2003-444649	A1	20030522 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-724479, filed on 28 Nov 2000, ABANDONED Division of Ser. No. US 2000-477923, filed on 5 Jan 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115010P	19990106 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 275 MIDDLEFIELD ROAD, MENLO PARK, CA, 94025-3506

NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2419

L7 ANSWER 7 OF 126 USPATFULL on STN
TI Modified proinsulin variants and composition containing same
AB IGF-I and insulin variants are provided that selectively bind to IGFBP-1 or IGFBP-3. These agonist variants are useful, for example, to improve the half-lives of IGF-I and insulin, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:31741 USPATFULL
TITLE: Modified proinsulin variants and composition containing same
INVENTOR(S): Dubaquie, Yves, San Francisco, CA, UNITED STATES
Lowman, Henry, El Granada, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2004023883	A1	20040205
APPLICATION INFO.:	US 2003-444262	A1	20030522 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-724478, filed on 28 Nov 2000, ABANDONED Division of Ser. No. US 2000-477923, filed on 5 Jan 2000, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1999-115010P	19990106 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HELLER EHRMAN WHITE & MCAULIFFE LLP, 275 MIDDLEFIELD ROAD, MENLO PARK, CA, 94025-3506
NUMBER OF CLAIMS: 49
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2420
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 8 OF 126 USPATFULL on STN
TI Alpha V integrin receptor antagonists
AB The present invention relates to novel alkanoic acid derivatives thereof, their synthesis, and their use as αv integrin receptor antagonists. More particularly, the compounds of the present invention are antagonists of the integrin receptors αvβ3 and/or αvβ5 and are useful for **inhibiting** bone resorption, treating and preventing osteoporosis, and **inhibiting** vascular restenosis, diabetic retinopathy, macular degeneration, **angiogenesis**, atherosclerosis, inflammatory arthritis, cancer, and metastatic tumor growth.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2004:25195 USPATFULL
TITLE: Alpha V integrin receptor antagonists
INVENTOR(S): Askew, Ben C., Newbury Park, CA, UNITED STATES
Breslin, Michael J., Drexel Hill, PA, UNITED STATES
Duggan, Mark E., Schwenksville, PA, UNITED STATES
Hutchinson, John H., Philadelphia, PA, UNITED STATES
Meissner, Robert S., Schwenksville, PA, UNITED STATES
Perkins, James J., Churchville, PA, UNITED STATES
Steele, Thomas G., Schwenksville, PA, UNITED STATES
Patane, Michael A., Billerica, MA, UNITED STATES

	NUMBER	KIND	DATE

PATENT INFORMATION:	US 2004019037	A1	20040129
APPLICATION INFO.:	US 2003-618414	A1	20030710 (10)
RELATED APPLN. INFO.:	Division of Ser. No. US 2001-767471, filed on 23 Jan 2001, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-177792P	20000124 (60)
	US 2000-230469P	20000906 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: MERCK AND CO INC, P O BOX 2000, RAHWAY, NJ, 070650907
NUMBER OF CLAIMS: 24
EXEMPLARY CLAIM: 1
LINE COUNT: 4146
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 9 OF 126 USPATFULL on STN
TI A2B adenosine receptor antagonists
AB Disclosed are novel compounds that are A.sub.2B adenosine receptor antagonists, useful for treating various disease states, including asthma and diarrhea.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:325124 USPATFULL
TITLE: A2B adenosine receptor antagonists
INVENTOR(S): Kalla, Rao, Mountain View, CA, UNITED STATES
Perry, Thao, San Jose, CA, UNITED STATES
Elzein, Elfatih, Fremont, CA, UNITED STATES
Varkhedkar, Vaibhav, San Diego, CA, UNITED STATES
Li, Xiaofen, Palo Alto, CA, UNITED STATES
Ibrahim, Prabha, Mountain View, CA, UNITED STATES
Palle, Venkata, Gurgaon, INDIA
Xiao, Dengming, Longmont, CO, UNITED STATES
Zablocki, Jeff, Mountain View, CA, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003229106	A1	20031211
APPLICATION INFO.:	US 2003-431167	A1	20030506 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2002-290921, filed on 8 Nov 2002, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2001-348222P	20011109 (60)
	US 2002-401408P	20020805 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: Brian Lewis, CV Therapeutics, Inc., 3172 Porter Drive, Palo Alto, CA, 94304
NUMBER OF CLAIMS: 32
EXEMPLARY CLAIM: 1
LINE COUNT: 3552
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 10 OF 126 USPATFULL on STN
TI Solid phase method for synthesis peptide-spacer-lipid conjugates, conjugates synthesized thereby and targeted liposomes containing the same
AB A solid phase synthesis method for preparing peptide-spacer-lipid conjugates, the peptide-spacer-lipid conjugates synthesized by the method, and liposomes containing the peptide-spacer-lipid conjugates.

The present invention provides a convenient solid phase synthesis method for preparing peptide-spacer-lipid conjugates and provides various linkage groups (such as amide group) for conjugating peptide, spacer and lipid, wherein the spacer may comprise PEG. Several advantages can be achieved, such as the synthetic procedure can be simplified, the synthesis process can be set to automation, the purification is easier in each reaction step, and the product losses can be reduced to minimal during synthesis. The present synthesis method is suitable for preparing a wide range of peptide-spacer-lipid conjugates, provides a peptide-spacer-lipid conjugate prepared by the solid phase synthesis method of the present invention, which can be incorporated into a liposome as the targeting moiety for liposomal drug delivery to specific cells, and provides a targeting liposome containing the present peptide-spacer-lipid conjugate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:325035 USPATFULL
TITLE:	Solid phase method for synthesis peptide-spacer-lipid conjugates, conjugates synthesized thereby and targeted liposomes containing the same
INVENTOR(S):	Wu, Shih-Kwang, Taipei, TAIWAN, PROVINCE OF CHINA Chang, Ting-Gung, Taipei, TAIWAN, PROVINCE OF CHINA Tseng, Chin-Lu, Taipei, TAIWAN, PROVINCE OF CHINA Chen, Li-Jung, Taipei, TAIWAN, PROVINCE OF CHINA Shih, Kae-Shyang, Taipei, TAIWAN, PROVINCE OF CHINA
PATENT ASSIGNEE(S):	DEVELOPMENT CENTER FOR BIOTECHNOLOGY (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003229017	A1	20031211
APPLICATION INFO.:	US 2002-308644	A1	20021203 (10)

RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-16569, filed on 7 Dec 2001, PENDING
DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	Ladas & Parry, 26 West 61st Street, New York, NY, 10023
NUMBER OF CLAIMS:	40
EXEMPLARY CLAIM:	1
LINE COUNT:	1774

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 11 OF 126 USPATFULL on STN

TI Solid phase method for synthesis peptide-spacer-lipid conjugates, conjugates synthesized thereby and targeted liposomes containing the same

AB A solid phase synthesis method for preparing peptide-spacer-lipid conjugates, the peptide-spacer-lipid conjugates synthesized by the method, and liposomes containing the peptide-spacer-lipid conjugates. The present invention provides a convenient solid phase synthesis method for preparing peptide-spacer-lipid conjugates and provides various linkage groups (such as amide group) for conjugating peptide, spacer and lipid, wherein the spacer may comprise PEG. Several advantages can be achieved, such as the synthetic procedure can be simplified, the synthesis process can be set to automation, the purification is easier in each reaction step, and the product losses can be reduced to minimal during synthesis. The present synthesis method is suitable for preparing a wide range of peptide-spacer-lipid conjugates, provides a peptide-spacer-lipid conjugate prepared by the solid phase synthesis method of the present invention, which can be incorporated into a liposome as the targeting moiety for liposomal drug delivery to specific cells, and provides a targeting liposome containing the present peptide-spacer-lipid conjugate.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:325031 USPATFULL
TITLE:	Solid phase method for synthesis peptide-spacer-lipid conjugates, conjugates synthesized thereby and targeted liposomes containing the same
INVENTOR(S):	Wu, Shih-Kwang, Taipei, TAIWAN, PROVINCE OF CHINA Chang, Ting-Gung, Taipei, TAIWAN, PROVINCE OF CHINA Tseng, Chin-Lu, Taipei, TAIWAN, PROVINCE OF CHINA Chen, Li-Jung, Taipei, TAIWAN, PROVINCE OF CHINA Shih, Kae-Shyang, Taipei, TAIWAN, PROVINCE OF CHINA

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003229013	A1	20031211
APPLICATION INFO.:	US 2001-16569	A1	20011207 (10)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	LARIVIERE, GRUBMAN & PAYNE, LLP, 1 LOWER RAGSDALE, BLDG. 1, SUITE 130, P.O. BOX 3140, MONTEREY, CA, 93942
NUMBER OF CLAIMS:	41
EXEMPLARY CLAIM:	1
LINE COUNT:	1670

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 12 OF 126 USPATFULL on STN

TI Novel human G-protein coupled receptor, HGPRBMY23, expressed highly in kidney

AB The present invention provides novel polynucleotides encoding HGPRBMY23 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel HGPRBMY23 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides, particularly renal diseases and/or disorders, colon cancer, breast cancer, and diseases and disorders related to aberrant NFKB modulation. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:318714 USPATFULL
TITLE:	Novel human G-protein coupled receptor, HGPRBMY23, expressed highly in kidney
INVENTOR(S):	Barber, Lauren E., Higganum, CT, UNITED STATES Cacace, Angela, Clinton, CT, UNITED STATES Feder, John N., Belle Mead, NJ, UNITED STATES Nelson, Thomas C., Lawrenceville, NJ, UNITED STATES Ramanathan, Chandra S., Wallingford, CT, UNITED STATES Ryseck, Rolf-Peter, Ewing, NJ, UNITED STATES Neubauer, Michael G., Skillman, NJ, UNITED STATES Kornacker, Michael G., Princeton, NJ, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003224458	A1	20031204
APPLICATION INFO.:	US 2003-375157	A1	20030226 (10)
RELATED APPLN. INFO.:	Continuation-in-part of Ser. No. US 2001-10568, filed on 7 Dec 2001, PENDING		

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-251926P	20001207 (60)
	US 2001-269795P	20010214 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 17 Drawing Page(s)
LINE COUNT: 14624
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 13 OF 126 USPATFULL on STN
TI Novel human G-protein coupled receptor, HGPRBMY11, and variants thereof
AB The present invention provides novel polynucleotides encoding HGPRBMY11 polypeptides, fragments and homologues thereof. The present invention also provides polynucleotides encoding variants of the HGPRBMY11 polypeptide, HGPRBMY11v1 and HGPRBMY11v2. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel HGPRBMY11, HGPRBMY11v1, and/or HGPRBMY11v2 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides, particularly gastrointestinal diseases and/or disorders, ovarian cancer, and diseases and disorders related to aberrant NFKB modulation. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:318656 USPATFULL
TITLE: Novel human G-protein coupled receptor, HGPRBMY11, and variants thereof
INVENTOR(S): Barber, Lauren E., Higganum, CT, UNITED STATES
Cacace, Angela, Clinton, CT, UNITED STATES
Feder, John N., Belle Mead, NJ, UNITED STATES
Nelson, Thomas C., Lawrenceville, NJ, UNITED STATES
Bol, David K., Gaithersburg, MD, UNITED STATES
Ramanathan, Chandra, Wallingford, CT, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003224400	A1	20031204
APPLICATION INFO.:	US 2003-369405	A1	20030214 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2001-991225, filed on 16 Nov 2001, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	US 2000-249613P	20001117 (60)
	US 2000-257611P	20001221 (60)
	US 2001-305818P	20010716 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 18 Drawing Page(s)
LINE COUNT: 15695
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 14 OF 126 USPATFULL on STN
TI Composition and imaging methods for pharmacokinetic and pharmacodynamic evaluation of therapeutic delivery system
AB A halogen-labeled gene therapy construct that includes halogen-labeled

nucleic acids, methods for preparing a halogenated gene therapy construct, and methods for in vivo imaging of the same. Also provided are methods for non-invasive drug detection in a subject using a labeled antibody that recognizes a heterologous antigen conjugated to, encoded by, or otherwise associated with the drug.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:306901 USPATFULL
TITLE:	Composition and imaging methods for pharmacokinetic and pharmacodynamic evaluation of therapeutic delivery system
INVENTOR(S):	Hallahan, Dennis E., Nashville, TN, UNITED STATES
PATENT ASSIGNEE(S):	Vanderbilt University (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003216337	A1	20031120
APPLICATION INFO.:	US 2003-342805	A1	20030115 (10)

	NUMBER	DATE
PRIORITY INFORMATION:	US 2002-348945P	20020115 (60)

DOCUMENT TYPE:	Utility
FILE SEGMENT:	APPLICATION
LEGAL REPRESENTATIVE:	JENKINS & WILSON, PA, 3100 TOWER BLVD, SUITE 1400, DURHAM, NC, 27707
NUMBER OF CLAIMS:	49
EXEMPLARY CLAIM:	1
NUMBER OF DRAWINGS:	3 Drawing Page(s)
LINE COUNT:	2902

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 15 OF 126 USPATFULL on STN

TI Novel fluorescence dyes and their applications for whole-cell fluorescence screening assays for caspases, peptidases, proteases and other enzymes and the use thereof

AB The present invention relates to novel fluorescent dyes, novel fluorogenic and fluorescent reporter molecules and new enzyme assay processes that can be used to detect the activity of caspases and other enzymes involved in apoptosis in whole cells, cell lines and tissue samples derived from any living organism or organ. The reporter molecules and assay processes can be used in drug screening procedures to identify compounds which act as **inhibitors** or inducers of the caspase cascade in whole cells or tissues. The reagents and assays described herein are also useful for determining the chemosensitivity of human cancer cells to treatment with chemotherapeutic drugs. The present invention also relates to novel fluorogenic and fluorescent reporter molecules and new enzyme assay processes that can be used to detect the activity of type 2 methionine aminopeptidase, HIV protease, adenovirus protease, HSV-1 protease, HCMV protease and HCV protease.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:295019 USPATFULL
TITLE:	Novel fluorescence dyes and their applications for whole-cell fluorescence screening assays for caspases, peptidases, proteases and other enzymes and the use thereof
INVENTOR(S):	Zhang, Han-Zhong, San Diego, CA, UNITED STATES Cai, Sui Xiong, San Diego, CA, UNITED STATES Drewe, John A., Carlsbad, CA, UNITED STATES Yang, Wu, Irvine, CA, UNITED STATES
PATENT ASSIGNEE(S):	Cytovia, Inc. (U.S. corporation)

	NUMBER	KIND	DATE

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003208037	A1	20031106
APPLICATION INFO.:	US 2002-138375	A1	20020506 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-583225, filed on 30 May 2000, ABANDONED Division of Ser. No. US 1999-357952, filed on 21 Jul 1999, GRANTED, Pat. No. US 6248904

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-93642P	19980721 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STERNE, KESSLER, GOLDSTEIN & FOX PLLC, 1100 NEW YORK AVENUE, N.W., WASHINGTON, DC, 20005
NUMBER OF CLAIMS: 73
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 9 Drawing Page(s)
LINE COUNT: 3991
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 16 OF 126 USPATFULL on STN

TI Methods of treating psoriatic arthritis with chimeric anti-TNF antibodies

AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-α (TNFα) and are useful in vivo diagnosis and therapy of a number of TNFα-mediated pathologies and conditions, as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:289305 USPATFULL
TITLE: Methods of treating psoriatic arthritis with chimeric anti-TNF antibodies
INVENTOR(S): Le, Junming, Jackson Heights, NY, UNITED STATES
Vilcek, Jan, New York, NY, UNITED STATES
Daddona, Peter, Menlo Park, CA, UNITED STATES
Ghrayeb, John, Downingtown, PA, UNITED STATES
Knight, David, Berwyn, PA, UNITED STATES
Siegel, Scott, Westborough, MA, UNITED STATES
PATENT ASSIGNEE(S): New York University, New York, NY (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003204066	A1	20031030
APPLICATION INFO.:	US 2003-371962	A1	20030221 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-756398, filed on 8 Jan 2001, PENDING Division of Ser. No. US 1998-133119, filed on 12 Aug 1998, GRANTED, Pat. No. US 6277969 Division of Ser. No. US 1995-570674, filed on 11 Dec 1995, ABANDONED Continuation-in-part of Ser. No. US 1994-324799, filed on 18 Oct 1994, GRANTED, Pat. No. US 5698195 Continuation-in-part of Ser. No. US 1994-192102, filed on 4 Feb 1994, GRANTED, Pat. No. US 5656272 Continuation-in-part of Ser. No. US 1994-192861, filed on 4 Feb 1994, GRANTED, Pat. No. US 5919452 Continuation-in-part of Ser. No. US 1994-192093, filed on 4 Feb 1994, GRANTED, Pat. No. US 6284471 Continuation-in-part of Ser. No. US 1993-10406, filed on 29 Jan 1993, ABANDONED Continuation-in-part of Ser. No. US 1993-13413, filed on 2 Feb 1993, ABANDONED Continuation-in-part of Ser. No. US 1992-943852, filed

on 11 Sep 1992, ABANDONED Continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, ABANDONED Continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 37 Drawing Page(s)
LINE COUNT: 5707
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 17 OF 126 USPATFULL on STN
TI Treatment of osteoarthritis
AB Agents with integrin-afffecting activity, including antibodies and molecules having the antigen-binding portion of such antibodies, are used to regulate inflammatory mediators, including TL-1β, IL-6, IL-8, nitric oxide, PGE.sub.2 and MMPs.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:288219 USPATFULL
TITLE: Treatment of osteoarthritis
INVENTOR(S): Amin, Ashok R., Union, NJ, UNITED STATES
Abramson, Steven, Rye, NY, UNITED STATES
Attur, Mukandan, Woodside, NY, UNITED STATES
PATENT ASSIGNEE(S): New York University, New York, NY (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003202977	A1	20031030
APPLICATION INFO.:	US 2003-461423	A1	20030616 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1999-441217, filed on 16 Nov 1999, ABANDONED

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-108521P	19981116 (60)
	US 1999-116966P	19990122 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: BROWDY AND NEIMARK, P.L.L.C., 624 NINTH STREET, NW, SUITE 300, WASHINGTON, DC, 20001-5303
NUMBER OF CLAIMS: 30
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 7 Drawing Page(s)
LINE COUNT: 2289
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 18 OF 126 USPATFULL on STN
TI Composition for the treatment of damaged tissue
AB A pharmaceutical for use in damaged tissue, such as wound, treatment (e.g. healing) is described. The pharmaceutical comprising a composition which comprises: (a) a growth factor; and (b) an **inhibitor** agent; and optionally (c) a pharmaceutically acceptable carrier, diluent or excipient; wherein the **inhibitor** agent can **inhibit** the action of at least one specific adverse protein (e.g. a specific protease) that is upregulated in a damaged tissue, such as a wound, environment.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:283096 USPATFULL
TITLE: Composition for the treatment of damaged tissue

INVENTOR(S): Dack, Kevin Neil, Kent, UNITED KINGDOM
Davies, Michael John, Kent, UNITED KINGDOM
Fish, Paul Vincent, Kent, UNITED KINGDOM
Huggins, Jonathan Paul, Kent, UNITED KINGDOM
McIntosh, Fraser Stuart, Kent, UNITED KINGDOM
Occleston, Nicholas Laurence, Kent, UNITED KINGDOM
PATENT ASSIGNEE(S): Pfizer Inc. (non-U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003199440	A1	20031023
APPLICATION INFO.:	US 2002-131985	A1	20020425 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2000-725295, filed on 29 Nov 2000, PENDING

	NUMBER	DATE
PRIORITY INFORMATION:	GB 1999-30768	19991229
	US 2000-186426P	20000302 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: PFIZER INC, 150 EAST 42ND STREET, 5TH FLOOR - STOP 49, NEW YORK, NY, 10017-5612
NUMBER OF CLAIMS: 29
EXEMPLARY CLAIM: 1
LINE COUNT: 19445
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 19 OF 126 USPATFULL on STN
TI Novel human G-protein coupled receptor, HGPRBMY14, related to the orphan GPCR, GPR73
AB The present invention provides novel polynucleotides encoding HGPRBMY14 polypeptides, fragments and homologues thereof. Also provided are vectors, host cells, antibodies, and recombinant and synthetic methods for producing said polypeptides. The invention further relates to diagnostic and therapeutic methods for applying these novel HGPRBMY14 polypeptides to the diagnosis, treatment, and/or prevention of various diseases and/or disorders related to these polypeptides. The invention further relates to screening methods for identifying agonists and antagonists of the polynucleotides and polypeptides of the present invention.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:282633 USPATFULL
TITLE: Novel human G-protein coupled receptor, HGPRBMY14, related to the orphan GPCR, GPR73
INVENTOR(S): Feder, John N., Belle Mead, NJ, UNITED STATES
Ramanathan, Chandra S., Wallingford, CT, UNITED STATES
Nelson, Thomas C., Lawrenceville, NJ, UNITED STATES
Kornacker, Michael G., Princeton, NJ, UNITED STATES
Ryseck, Rolf-Peter, Ewing, CT, UNITED STATES
Cacace, Angela, Clinton, CT, UNITED STATES
Barber, Lauren E., Higganum, CT, UNITED STATES
Bol, David K., Gaithersburg, MD, UNITED STATES

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003198976	A1	20031023
APPLICATION INFO.:	US 2002-295693	A1	20021114 (10)

RELATED APPLN. INFO.: Continuation-in-part of Ser. No. US 2002-67649, filed on 5 Feb 2002, PENDING

	NUMBER	DATE

PRIORITY INFORMATION: US 2001-266525P 20010205 (60)
US 2001-329897P 20011016 (60)
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: STEPHEN B. DAVIS, BRISTOL-MYERS SQUIBB COMPANY, PATENT DEPARTMENT, P O BOX 4000, PRINCETON, NJ, 08543-4000
NUMBER OF CLAIMS: 26
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 16 Drawing Page(s)
LINE COUNT: 15175
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 20 OF 126 USPATFULL on STN
TI Methods of treating ulcerative colitis with chimeric anti-TNF antibodies
AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-α (TNFα) and are useful in vivo diagnosis and therapy of a number of TNFα-mediated pathologies and conditions, as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:282300 USPATFULL
TITLE: Methods of treating ulcerative colitis with chimeric anti-TNF antibodies
INVENTOR(S): Le, Junming, Jackson Heights, NY, UNITED STATES
Vilcek, Jan, New York, NY, UNITED STATES
Daddona, Peter, Menlo Park, CA, UNITED STATES
Ghraveb, John, Downingtown, PA, UNITED STATES
Knight, David, Berwyn, PA, UNITED STATES
Siegel, Scott, Westborough, MA, UNITED STATES
PATENT ASSIGNEE(S): New York University, New York, NY (U.S. corporation)
Centocor, Inc., Malvern, PA (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003198641	A1	20031023
APPLICATION INFO.:	US 2003-379866	A1	20030304 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-756398, filed on 8 Jan 2001, PENDING Division of Ser. No. US 1998-133119, filed on 12 Aug 1998, GRANTED, Pat. No. US 6277969 Division of Ser. No. US 1995-570674, filed on 11 Dec 1995, ABANDONED Continuation-in-part of Ser. No. US 1994-324799, filed on 18 Oct 1994, GRANTED, Pat. No. US 5698195 Continuation-in-part of Ser. No. US 1994-192102, filed on 4 Feb 1994, GRANTED, Pat. No. US 5656272 Continuation-in-part of Ser. No. US 1994-192861, filed on 4 Feb 1994, GRANTED, Pat. No. US 5919452 Continuation-in-part of Ser. No. US 1994-192093, filed on 4 Feb 1994, GRANTED, Pat. No. US 6284471 Continuation-in-part of Ser. No. US 1993-10406, filed on 29 Jan 1993, ABANDONED Continuation-in-part of Ser. No. US 1993-13413, filed on 2 Feb 1993, ABANDONED Continuation-in-part of Ser. No. US 1992-943852, filed on 11 Sep 1992, ABANDONED Continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, ABANDONED Continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
NUMBER OF CLAIMS: 26

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 37 Drawing Page(s)
LINE COUNT: 5737
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 21 OF 126 USPATFULL on STN
TI Methods of treating joint inflammation with chimeric anti-TNF antibodies
AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-α (TNFα) and are useful in vivo diagnosis and therapy of a number of TNFα-mediated pathologies and conditions, as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:282293 USPATFULL
TITLE: Methods of treating joint inflammation with chimeric anti-TNF antibodies
INVENTOR(S): Le, Junming, Jackson Heights, NY, UNITED STATES
Vilcek, Jan, New York, NY, UNITED STATES
Daddona, Peter, Menlo Park, CA, UNITED STATES
Ghrayeb, John, Downingtown, PA, UNITED STATES
Knight, David, Berwyn, PA, UNITED STATES
Siegel, Scott, Westborough, MA, UNITED STATES
PATENT ASSIGNEE(S): New York University, New York, NY (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003198634	A1	20031023
APPLICATION INFO.:	US 2003-371443	A1	20030221 (10)

RELATED APPLN. INFO.: Division of Ser. No. US 2001-756398, filed on 8 Jan 2001, PENDING Division of Ser. No. US 1998-133119, filed on 12 Aug 1998, GRANTED, Pat. No. US 6277969 Division of Ser. No. US 1995-570674, filed on 11 Dec 1995, ABANDONED Continuation-in-part of Ser. No. US 1994-324799, filed on 18 Oct 1994, GRANTED, Pat. No. US 5698195 Continuation-in-part of Ser. No. US 1994-192102, filed on 4 Feb 1994, GRANTED, Pat. No. US 5656272 Continuation-in-part of Ser. No. US 1994-192861, filed on 4 Feb 1994, GRANTED, Pat. No. US 5919452 Continuation-in-part of Ser. No. US 1994-192093, filed on 4 Feb 1994, GRANTED, Pat. No. US 6284471 Continuation-in-part of Ser. No. US 1993-10406, filed on 29 Jan 1993, ABANDONED Continuation-in-part of Ser. No. US 1993-13413, filed on 2 Feb 1993, ABANDONED Continuation-in-part of Ser. No. US 1992-943852, filed on 11 Sep 1992, ABANDONED Continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, ABANDONED Continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
NUMBER OF CLAIMS: 28
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 37 Drawing Page(s)
LINE COUNT: 5740
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 22 OF 126 USPATFULL on STN
TI Methods of sustained treatment of fistulas in crohn's disease with chimeric anti-TNF antibodies

AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-α (TNFα) and are useful in vivo diagnosis and therapy of a number of TNFα-mediated pathologies and conditions, as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER: 2003:276377 USPATFULL

TITLE: Methods of sustained treatment of fistulas in crohn's disease with chimeric anti-TNF antibodies

INVENTOR(S): Le, Junming, Jackson Heights, NY, UNITED STATES
Vilcek, Jan, New York, NY, UNITED STATES
Daddona, Peter, Menlo Park, CA, UNITED STATES
Ghrayeb, John, Thorndale, PA, UNITED STATES
Knight, David, Berwyn, PA, UNITED STATES
Siegel, Scott, Westborough, MA, UNITED STATES

PATENT ASSIGNEE(S): New York University, New York, NY, UNITED STATES (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003194402	A1	20031016
APPLICATION INFO.:	US 2002-319011	A1	20021212 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-756398, filed on 8 Jan 2001, PENDING Division of Ser. No. US 1998-133119, filed on 12 Aug 1998, GRANTED, Pat. No. US 6277969 Division of Ser. No. US 1995-570674, filed on 11 Dec 1995, ABANDONED Continuation-in-part of Ser. No. US 1994-324799, filed on 18 Oct 1994, GRANTED, Pat. No. US 5698195 Continuation-in-part of Ser. No. US 1994-192102, filed on 4 Feb 1994, GRANTED, Pat. No. US 5656272 Continuation-in-part of Ser. No. US 1994-192861, filed on 4 Feb 1994, GRANTED, Pat. No. US 5919452 Continuation-in-part of Ser. No. US 1994-192093, filed on 4 Feb 1994, GRANTED, Pat. No. US 6284471 Continuation-in-part of Ser. No. US 1993-10406, filed on 29 Jan 1993, ABANDONED Continuation-in-part of Ser. No. US 1993-13413, filed on 2 Feb 1993, ABANDONED Continuation-in-part of Ser. No. US 1992-943852, filed on 11 Sep 1992, ABANDONED Continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, ABANDONED Continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, ABANDONED

DOCUMENT TYPE: Utility

FILE SEGMENT: APPLICATION

LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133

NUMBER OF CLAIMS: 38

EXEMPLARY CLAIM: 1

NUMBER OF DRAWINGS: 37 Drawing Page(s)

LINE COUNT: 5700

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 23 OF 126 USPATFULL on STN

TI Non-peptide somatostatin receptor ligands

AB Non-peptide somatostatin receptor ligands with conformationally restricted side chains exhibiting high binding affinity toward somatostatin receptors are provided. The compounds exhibit a high selectivity and act as agonists at human subtype 2 somatostatin receptors. The compounds are long acting for advantageous use as medicaments in peripheral diseases where somatostatinergic therapy is indicated. Furthermore, many of the compounds are lipophilic and are

particularly useful for treating central nervous system and ophthalmic diseases where penetration of the blood brain and blood retinal barriers is required. It is a further object to describe the preferred stereoisomers of these somatostatin agonists and processes for their preparation. Further objects will become apparent from reading the following description.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:271526 USPATFULL		
TITLE:	Non-peptide somatostatin receptor ligands		
INVENTOR(S):	Shapiro, Gideon, Gainesville, FL, UNITED STATES Natchus, Michael G., Alpharetta, GA, UNITED STATES Lockwood, Mark A., Alpharetta, GA, UNITED STATES Jurczyk, Simona, Gainesville, FL, UNITED STATES		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003191134	A1	20031009
APPLICATION INFO.:	US 2002-289924	A1	20021107 (10)
	NUMBER		DATE
PRIORITY INFORMATION:	US 2001-344564P		20011228 (60)
	US 2001-344563P		20011228 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	SALIWANCHIK LLOYD & SALIWANCHIK, A PROFESSIONAL ASSOCIATION, 2421 N.W. 41ST STREET, SUITE A-1, GAINESVILLE, FL, 326066669		
NUMBER OF CLAIMS:	59		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	2 Drawing Page(s)		
LINE COUNT:	2078		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 24 OF 126 USPATFULL on STN

TI Modified proinsulin variants and composition containing same

AB IGF-I and insulin variants are provided that selectively bind to IGFBP-1 or IGFBP-3. These agonist variants are useful, for example, to improve the half-lives of IGF-I and insulin, respectively.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:271458 USPATFULL		
TITLE:	Modified proinsulin variants and composition containing same		
INVENTOR(S):	Dubaquie, Yves, San Francisco, CA, UNITED STATES Lowman, Henry, El Granada, CA, UNITED STATES		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003191065	A1	20031009
APPLICATION INFO.:	US 2003-444326	A1	20030522 (10)
RELATED APPLN. INFO.:	Continuation of Ser. No. US 2000-723866, filed on 28 Nov 2000, ABANDONED Division of Ser. No. US 2000-477923, filed on 5 Jan 2000, ABANDONED		
	NUMBER		DATE
PRIORITY INFORMATION:	US 1999-115010P		19990106 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	HELLER EHRMAN WHITE & MCAULIFFE LLP, 275 MIDDLEFIELD ROAD, MENLO PARK, CA, 94025-3506		
NUMBER OF CLAIMS:	49		

EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 6 Drawing Page(s)
LINE COUNT: 2418
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L7 ANSWER 25 OF 126 USPATFULL on STN
TI Humanized anti-TNF antibodies and peptides
AB Anti-TNF antibodies, fragments and regions thereof which are specific for human tumor necrosis factor-α (TNFα) and are useful in vivo diagnosis and therapy of a number of TNFα-mediated pathologies and conditions, as well as polynucleotides coding for murine and chimeric antibodies, methods of producing the antibody, methods of use of the anti-TNF antibody, or fragment, region or derivative thereof, in immunoassays and immunotherapeutic approaches are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER: 2003:266214 USPATFULL
TITLE: Humanized anti-TNF antibodies and peptides
INVENTOR(S): Le, Junming, Jackson Heights, NY, UNITED STATES
Vilcek, Jan, New York, NY, UNITED STATES
Daddona, Peter, Menlo Park, CA, UNITED STATES
Ghrayeb, John, Downingtown, PA, UNITED STATES
Knight, David, Berwyn, PA, UNITED STATES
Siegel, Scott, Westborough, MA, UNITED STATES
PATENT ASSIGNEE(S): New York University, New York, NY (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003187231	A1	20031002
APPLICATION INFO.:	US 2002-200795	A1	20020722 (10)

RELATED APPLN. INFO.: Continuation of Ser. No. US 2001-756398, filed on 8 Jan 2001, PENDING Division of Ser. No. US 1998-133119, filed on 12 Aug 1998, GRANTED, Pat. No. US 6277969 Division of Ser. No. US 1995-570674, filed on 11 Dec 1995, ABANDONED Continuation-in-part of Ser. No. US 1994-324799, filed on 18 Oct 1994, GRANTED, Pat. No. US 5698195 Continuation-in-part of Ser. No. US 1994-192102, filed on 4 Feb 1994, GRANTED, Pat. No. US 5656272 Continuation-in-part of Ser. No. US 1994-192861, filed on 4 Feb 1994, GRANTED, Pat. No. US 5919452 Continuation-in-part of Ser. No. US 1994-192093, filed on 4 Feb 1994, GRANTED, Pat. No. US 6284471 Continuation-in-part of Ser. No. US 1993-10406, filed on 29 Jan 1993, ABANDONED Continuation-in-part of Ser. No. US 1993-13413, filed on 2 Feb 1993, ABANDONED Continuation-in-part of Ser. No. US 1992-943852, filed on 11 Sep 1992, ABANDONED Continuation-in-part of Ser. No. US 1992-853606, filed on 18 Mar 1992, ABANDONED Continuation-in-part of Ser. No. US 1991-670827, filed on 18 Mar 1991, ABANDONED
DOCUMENT TYPE: Utility
FILE SEGMENT: APPLICATION
LEGAL REPRESENTATIVE: HAMILTON, BROOK, SMITH & REYNOLDS, P.C., 530 VIRGINIA ROAD, P.O. BOX 9133, CONCORD, MA, 01742-9133
NUMBER OF CLAIMS: 62
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 37 Drawing Page(s)
LINE COUNT: 5880
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> e McCrae, K/au
E1 1 MCCRAE WILLIAM/AU
E2 1 MCCRAE WILLIAM H/AU

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E3            0 --> MCCRAE, K/AU
E4            1     MCCRAIG C D/AU
E5            1     MCCRAIG D J/AU
E6            1     MCCRAIG J/AU
E7            1     MCCRAIG R/AU
E8            1     MCCRAIG ROBERT/AU
E9            1     MCCRAIN G R/AU
E10           1     MCCRAINE J D/AU
E11           2     MCCRAINE N/AU
E12           1     MCCRAINIE J/AU

=> s kinnogen
L12           1 KINNOGEN

=> d l12 ti abs ibib tot

L12  ANSWER 1 OF 1  EMBASE  COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED.
     on STN
TI   Purification of high molecular weight kininogen and the role of this agent
     in blood coagulation.
AB   Recent studies of individuals with high molecular weight (HMW) kininogen
     deficiency established the importance of this plasma protein for in vitro
     initiation of blood coagulation. In the present study, HMW-kininogen was
     highly purified from human plasma by monitoring its clot-promoting
     activity, using Fitzgerald trait plasma as a substrate. This preparation
     of HMW-kininogen revealed a single band on sodium dodecyl
     sulfate-polyacrylamide gel electrophoresis (mol wt: 120,000) and released
     1% of its weight as bradykinin upon incubation with plasma kallikrein.
     HMW-kininogen specifically repaired impaired surface-mediated plasma
     reactions of Fitzgerald trait plasma, but did not affect those of Hageman
     trait and Fletcher trait plasma. Kinin release from HMW-kinnogen
     by trypsin, but not by plasma kallikrein, resulted in total loss of clot
     promoting activity. No inhibitors of coagulation were found when all kinin
     activity was removed from HMW-kininogen by trypsin. The roles of
     HMW-kininogen, Hageman factor (HF, Factor XII), plasma prekallikrein
     (Fletcher factor), and plasma thromboplastin antecedent (PTA, Factor XI)
     in blood coagulation were studied in a purified system. HMW-kininogen was
     absolutely required for activation of PTA by HF and ellagic acid. The
     yield of activated PTA was proportional to the amount of HF,
     HMW-kininogen, and PTA in the mixtures, suggesting that, to activate PTA,
     these three proteins might form a complex in the presence of ellagic acid.
     No fragmentation of HF was found under these conditions. In contrast to
     HF, HF-fragments (mol wt: 30,000) activated PTA in the absence of
     HMW-kininogen and ellagic acid. Thus, it appears that in the present study
     PTA was activated in two distinct ways. Which pathway is the major one in
     whole plasma remains to be determined.
ACCESSION NUMBER:    78181455  EMBASE
DOCUMENT NUMBER:     1978181455
TITLE:               Purification of high molecular weight kininogen and the
                     role of this agent in blood coagulation.
AUTHOR:              Saito H.
CORPORATE SOURCE:    Dept. Med., Sch. Med., Case West. Reserve Univ., Cleveland,
                     Ohio 44106, United States
SOURCE:              Journal of Clinical Investigation, (1977) 60/3 (584-594).
                     CODEN: JCINAO
COUNTRY:             United States
DOCUMENT TYPE:       Journal
FILE SEGMENT:        037     Drug Literature Index
                     025     Hematology
                     029     Clinical Biochemistry
                     030     Pharmacology
LANGUAGE:            English
```

```
=> s kininogen
L13         4827 KININOGEN

=> d his

     (FILE 'HOME' ENTERED AT 09:39:19 ON 08 MAR 2004)

     FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA' ENTERED AT 09:41:44
     ON 08 MAR 2004
L1         182982 S ANGIOGENESIS
L2          87878 S L1 AND INHIBIT?
L3              0 S (CYTOKINE DRIVEN INHIBITION) AND ANGIOGENESIS
L4          16803 S L2 AND CYTOKINE
L5              0 S L4 AND CARBOBENZYBXY GROUP
L6           6215 S T-BUTYLOXYCARBONYL
L7            126 S L6 AND L4
L8           7254 S HK
L9            241 S HKA
L10            64 S L8 AND L9
L11             0 S L10 AND L7
                E MCCRAE, K/AU
L12             1 S KINNOGEN
L13          4827 S KININOGEN

=> s l13 and l1
L14          196 L13 AND L1

=> s l2 and l14
L15          185 L2 AND L14

=> s l15 and l6
L16            1 L15 AND L6

=> d l16 ti abs ibib tot

L16  ANSWER 1 OF 1  USPATFULL on STN
TI     Inhibition of angiogenesis by peptide analogs of
       high molecular weight kininogen domain 5
AB     Peptide analogs of the high molecular weight kininogen domain
       5 are potent inhibitors of angiogenesis. The
       peptides have the formula

       X.sub.1 -(HGLGHGHEQQHGKGH)-X.sub.2  (I)

       wherein

       X.sub.1 is from zero to 25 amino acids;

       X.sub.2 is from zero to 60 amino acids.

       Methods of inhibiting endothelial cell proliferation and
       angiogenesis are provided.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.
ACCESSION NUMBER:         2001:147934  USPATFULL
TITLE:                    Inhibition of angiogenesis by
                          peptide analogs of high molecular weight
                          kininogen domain 5
INVENTOR(S):              Colman, Robert W., Media, PA, United States
                          Mousa, Shaker A., New London, PA, United States
PATENT ASSIGNEE(S):       Temple University - Of The Commonwealth System of
                          Higher Education, Philadelphia, PA, United States (U.S.
                          corporation)
                          Du Pont Pharmaceuticals Company, Wilmington, DE, United
```

States (U.S. corporation)

	NUMBER	KIND	DATE
PATENT INFORMATION:	US 6284726	B1	20010904
APPLICATION INFO.:	US 2000-612126		20000707 (9)
RELATED APPLN. INFO.:	Continuation of Ser. No. WO 1999-US26377, filed on 9 Nov 1999		

	NUMBER	DATE
PRIORITY INFORMATION:	US 1998-107844P	19981110 (60)

DOCUMENT TYPE: Utility
FILE SEGMENT: GRANTED
PRIMARY EXAMINER: Carlson, Karen Cochrane
ASSISTANT EXAMINER: Robinson, Patricia
LEGAL REPRESENTATIVE: Drinker Biddle & Reath LLP
NUMBER OF CLAIMS: 25
EXEMPLARY CLAIM: 1
NUMBER OF DRAWINGS: 4 Drawing Figure(s); 1 Drawing Page(s)
LINE COUNT: 801
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

=> d his

(FILE 'HOME' ENTERED AT 09:39:19 ON 08 MAR 2004)

FILE 'MEDLINE, USPATFULL, DGENE, EMBASE, WPIDS, FSTA' ENTERED AT 09:41:44 ON 08 MAR 2004

```
L1        182982 S ANGIOGENESIS
L2         87878 S L1 AND INHIBIT?
L3             0 S (CYTOKINE DRIVEN INHIBITION) AND ANGIOGENESIS
L4         16803 S L2 AND CYTOKINE
L5             0 S L4 AND CARBOBENZYBXY GROUP
L6          6215 S T-BUTYLOXYCARBONYL
L7           126 S L6 AND L4
L8          7254 S HK
L9           241 S HKA
L10           64 S L8 AND L9
L11            0 S L10 AND L7
                 E MCCRAE, K/AU
L12            1 S KINNOGEN
L13         4827 S KININOGEN
L14          196 S L13 AND L1
L15          185 S L2 AND L14
L16            1 S L15 AND L6
```

=> s l15 and l9
L17 32 L15 AND L9

=> d l17 ti abs ibib tot

L17 ANSWER 1 OF 32 MEDLINE on STN
TI **Inhibition** of **angiogenesis** by antibody blocking the action of proangiogenic high-molecular-weight **kininogen**.
AB Previously we demonstrated that domain 5 (D5) of high-molecular-weight **kininogen** (HK) **inhibits** neovascularization in the chicken chorioallantoic membrane (CAM) assay and further found that kallikrein cleaved HK (**HKa**) **inhibited** FGF2-and VEGF-induced neovascularization, and thus was antiangiogenic. In this study, we sought to demonstrate whether uncleaved HK stimulates neovascularization and thus is proangiogenic. The chick chorioallantoic membrane was used as an in ovo assay of **angiogenesis**.

Low-molecular-weight **kininogen** stimulates **angiogenesis**, indicating that D5 is not involved. Bradykinin stimulates neovascularization equally to HK and LK and is likely to be responsible for the effect of HK. A murine monoclonal antibody to HK (C11C1) also recognizes a similar component in chicken plasma as detected by surface plasmon resonance. **Angiogenesis** induced by FGF2 and VEGF is **inhibited** by this monoclonal antibody and is a more potent **inhibitor** of neovascularization induced by VEGF than an integrin alphavbeta3 antibody (LM 609). Our postulate that C11C1 **inhibits** the stimulation of **angiogenesis** by HK was confirmed when either C11C1 or D5 completely **inhibited angiogenesis** in the CAM induced by HK. Growth of human fibrosarcoma (HT-1080) on the CAM was **inhibited** by GST-D5 and C11C1. These results indicate HK is proangiogenic probably by releasing bradykinin and that a monoclonal antibody directed to HK could serve as an antiangiogenic agent with a potential for **inhibiting** tumor **angiogenesis** and other **angiogenesis**-mediated disorders.

ACCESSION NUMBER: 2003339508 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12871554
TITLE: **Inhibition** of **angiogenesis** by antibody blocking the action of proangiogenic high-molecular-weight **kininogen**.
AUTHOR: Colman R W; Pixley R A; Sainz I M; Song J S; Isordia-Salas I; Muhamed S N; Powell J A Jr; Mousa S A
CORPORATE SOURCE: The Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA 19140, USA.. robert.colman@temple.edu
CONTRACT NUMBER: P01 HL56914 (NHLBI)
R01 CA63938 (NCI)
SOURCE: Journal of thrombosis and haemostasis : JTH, (2003 Jan) 1 (1) 164-70.
Journal code: 101170508. ISSN: 1538-7933.
PUB. COUNTRY: England: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200310
ENTRY DATE: Entered STN: 20030722
Last Updated on STN: 20031009
Entered Medline: 20031008

L17 ANSWER 2 OF 32 MEDLINE on STN
TI Apoptotic effect of cleaved high molecular weight **kininogen** is regulated by extracellular matrix proteins.
AB We previously reported that cleaved high molecular weight **kininogen** (**HKa**) and its domain 5 (D5) **inhibit** critical steps required for **angiogenesis** and in vivo neovascularization (Colman et al. 2000: Blood 95:543-550). We have further shown that D5 is able to induce apoptosis of endothelial cells, which may represent a critical part of the anti-angiogenic activity of **HKa** and D5 (Guo et al. 2001: Arterioscler Thromb Vasc Biol 21:1427-1433). In this study, we demonstrate that **HKa**- and D5-induced apoptosis is closely correlated with their anti-adhesive effect. An important new finding is that the apoptotic activity of **HKa** and D5 is highly regulated by their interactions with different extracellular matrix (ECM) proteins. **HKa** **inhibited** cell adhesion to vitronectin (Vn, 90%) and gelatin (Gel) (40%), but it had no apparent effect on cell adhesion to fibronectin (Fn). D5 showed a similar pattern on cell adhesion but was less potent than **HKa**. **HKa** induced apoptosis of endothelial cells grown on Vn and Gel but not cells grown on Fn which closely parallels with its anti-adhesive potency. Further results revealed that the anti-adhesive effect and the apoptotic effect of **HKa** are associated with its ability to **inhibit** phosphorylation of focal adhesion kinase

(FAK) and paxillin, two important signal molecules required for cell adhesion and cell viability. We conclude that the anti-adhesive activity of **HKa** and D5 is responsible for their apoptotic effect and that Vn is likely an ECM component that mediates the effect of **HKa** and D5.

ACCESSION NUMBER: 2003239267 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12761895
TITLE: Apoptotic effect of cleaved high molecular weight **kininogen** is regulated by extracellular matrix proteins.
AUTHOR: Guo Yan-Lin; Wang Shujie; Cao Dian J; Colman Robert W
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, Pennsylvania 19140, USA.. yguo0002@astro.temple.edu
CONTRACT NUMBER: P01 HL56914 (NHLBI)
R01 CA63938 (NCI)
SOURCE: Journal of cellular biochemistry, (2003 Jun 1) 89 (3) 622-32.
Journal code: 8205768. ISSN: 0730-2312.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200311
ENTRY DATE: Entered STN: 20030523
Last Updated on STN: 20031113
Entered Medline: 20031112

L17 ANSWER 3 OF 32 MEDLINE on STN
TI Upregulation of Cdc2 and cyclin A during apoptosis of endothelial cells induced by cleaved high-molecular-weight **kininogen**.
AB We (8) reported that the cleaved high-molecular-weight **kininogen** (**HKa**) and its domain 5 (D5) **inhibited angiogenesis**. Further studies (15) revealed that D5 could **inhibit** cell proliferation and induce apoptosis of proliferating endothelial cells, which together may represent a critical part of antiangiogenic activity of **HKa** and D5. In the present study, we further examined the effect of **HKa** on cell cycle progression and cell viability. We report that **HKa** induced a significant upregulation of Cdc2 and cyclin A in proliferating endothelial cells, concurrent with a marked increase of Cdc2 activity. The increased expression of Cdc2 and cyclin A by **HKa** was not associated with an apparent change in cell cycle profiles of basic fibroblast growth factor-stimulated proliferating cells, but closely correlated with a marked increase of apoptosis, suggesting that the elevated Cdc2 activity is involved in **HKa**-induced apoptosis of proliferating endothelial cells. Our results support an emerging hypothesis that Cdc2 and cyclin A are important regulators for cell cycle as well as for apoptosis.

ACCESSION NUMBER: 2003220752 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12742823
TITLE: Upregulation of Cdc2 and cyclin A during apoptosis of endothelial cells induced by cleaved high-molecular-weight **kininogen**.
AUTHOR: Wang Shujie; Hasham Muneer G; Isordia-Salas Irma; Tsygankov Alexander Y; Colman Robert W; Guo Yan-Lin
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, Pennsylvania 19140, USA.
CONTRACT NUMBER: P01-HL-56914 (NHLBI)
R01-CA-63938 (NCI)
R01-CA-78499 (NCI)
SOURCE: American journal of physiology. Heart and circulatory physiology, (2003 Jun) 284 (6) H1917-23.

Journal code: 100901228. ISSN: 0363-6135.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200306
ENTRY DATE: Entered STN: 20030514
Last Updated on STN: 20030621
Entered Medline: 20030620

L17 ANSWER 4 OF 32 MEDLINE on STN
TI Kininostatin as an antiangiogenic **inhibitor**: what we know and what we do not know.
AB High-molecular-weight **kininogen** (HK) is a plasma protein consisting of six domains (designated D1-D6). It was first characterized as a precursor of bradykinin, a bioactive peptide that regulates many cardiovascular processes. HK can bind to endothelial cells where it can be cleaved by plasma kallikrein to release bradykinin contained within domain 4. The remaining portion of the molecule, cleaved HK, is designated **HKa**. While bradykinin has been intensively studied, the physiological implication of the generation of **HKa** is not clear. **HKa** has recently been shown to **inhibit** the important steps required for **angiogenesis** such as proliferation and migration of endothelial cells. The antiangiogenic activity of **HKa** has further been demonstrated in animal models in which **HKa inhibits** neovascularization. Because domain 5 (D5) of **HKa** reproduces the antiangiogenic effect of **HKa**, D5 is named kininostatin for this novel function. In this review, we will briefly discuss the recent progress in the studies of the molecular mechanisms that mediate the antiangiogenic effect of **HKa** and D5.
ACCESSION NUMBER: 2002727083 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12489806
TITLE: Kininostatin as an antiangiogenic **inhibitor**: what we know and what we do not know.
AUTHOR: Guo Yan-Lin; Wang Shujie; Colman Robert W
CORPORATE SOURCE: The Sol Sherry Thrombosis Research Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, USA.. yguo0002@astro.temple.edu
CONTRACT NUMBER: P01 HL56914 (NHLBI)
R01 CA63938 (NCI)
SOURCE: International immunopharmacology, (2002 Dec) 2 (13-14) 1931-40. Ref: 66
Journal code: 100965259. ISSN: 1567-5769.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20021220
Last Updated on STN: 20030809
Entered Medline: 20030808

L17 ANSWER 5 OF 32 MEDLINE on STN
TI **Inhibition** of **angiogenesis** by a monoclonal antibody to **kininogen** as well as by kininostatin which block proangiogenic high molecular weight **kininogen**.
AB High molecular weight **kininogen** (HK) exhibits two activities with respect to **angiogenesis** after cleavage by plasma kallikrein. Cleaved HK (**HKa**) and its cell-binding domain 5 (D5), kininostatin, are potent antiangiogenic polypeptides. They **inhibit** endothelial cell migration, proliferation and tube formation. **HKa** and D5 **inhibit angiogenesis**

in the chicken chorioallantoic membrane (CAM) assay. D5 stimulates apoptosis and interferes with the cell cycle. In contrast, intact HK is proangiogenic by liberating bradykinin. A monoclonal antibody to HK can **inhibit angiogenesis** in the CAM assay, human colon carcinoma growing as a xenograft in nude mice, and murine hybridomas growing in syngeneic hosts. Not only are the tumors decreased in volume and weight to isotype controls but the mean vascular density is decreased. Thus, both D5 and its constituent peptide and monoclonal antibody have potential for **inhibiting angiogenesis** and tumor growth in human therapy.

ACCESSION NUMBER: 2002727079 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12489802
TITLE: **Inhibition** of **angiogenesis** by a monoclonal antibody to **kininogen** as well as by kininostatin which block proangiogenic high molecular weight **kininogen**.
AUTHOR: Colman Robert W
CORPORATE SOURCE: The Sol Sherry Thrombosis Research Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, USA.. colmanr@astro.temple.edu
SOURCE: International immunopharmacology, (2002 Dec) 2 (13-14) 1887-94. Ref: 17
Journal code: 100965259. ISSN: 1567-5769.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200308
ENTRY DATE: Entered STN: 20021220
Last Updated on STN: 20030809
Entered Medline: 20030808

L17 ANSWER 6 OF 32 MEDLINE on STN
TI The antiangiogenic activity of cleaved high molecular weight **kininogen** is mediated through binding to endothelial cell tropomyosin.
AB Conformationally altered proteins and protein fragments derived from the extracellular matrix and hemostatic system may function as naturally occurring **angiogenesis inhibitors**. One example of such a protein is cleaved high molecular weight **kininogen** (**HKa**). **HKa inhibits angiogenesis** by inducing apoptosis of proliferating endothelial cells, effects mediated largely by **HKa** domain 5. However, the mechanisms underlying the antiangiogenic activity of **HKa** have not been characterized, and its binding site on proliferating endothelial cells has not been defined. Here, we report that the induction of endothelial cell apoptosis by **HKa**, as well as the antiangiogenic activity of **HKa** in the chick chorioallantoic membrane, was **inhibited** completely by antitropomyosin monoclonal antibody TM-311. TM-311 also blocked the high-affinity Zn2+-dependent binding of **HKa** to both purified tropomyosin and proliferating endothelial cells. Confocal microscopic analysis of endothelial cells stained with monoclonal antibody TM-311, as well as biotin labeling of cell surface proteins on intact endothelial cells, revealed that tropomyosin exposure was enhanced on the surface of proliferating cells. These studies demonstrate that the antiangiogenic effects of **HKa** depend on high-affinity binding to endothelial cell tropomyosin.

ACCESSION NUMBER: 2002475716 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12196635
TITLE: The antiangiogenic activity of cleaved high molecular weight **kininogen** is mediated through binding to endothelial cell tropomyosin.

AUTHOR: Zhang Jing-Chuan; Donate Fernando; Qi Xiaoping; Ziats Nicholas P; Juarez Jose C; Mazar Andrew P; Pang Yuan-Ping; McCrae Keith R
CORPORATE SOURCE: Division of Hematology-Oncology, Case Western Reserve University School of Medicine and University Hospitals of Cleveland, Cleveland, OH 44106, USA.
CONTRACT NUMBER: R01 CA83134 (NCI)
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (2002 Sep 17) 99 (19) 12224-9. Journal code: 7505876. ISSN: 0027-8424.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020919
Last Updated on STN: 20030105
Entered Medline: 20021028

L17 ANSWER 7 OF 32 MEDLINE on STN
TI Histidine-proline-rich glycoprotein has potent antiangiogenic activity mediated through the histidine-proline-rich domain.
AB Histidine-proline-rich glycoprotein (HPRG) is an abundant multidomain plasma protein evolutionarily related to high-molecular-weight **kininogen**. The cleaved form of high-molecular-weight **kininogen** has recently been demonstrated to exhibit antiangiogenic activities in vitro (J. C. Zhang et al., FASEB J., 14: 2589-2600, 2000), mediated primarily through domain 5. HPRG contains a histidine-proline-rich (H/P) domain with sequence and functional similarities to **HKa** -D5. We hypothesized that HPRG may also have antiangiogenic properties, localized within its H/P domain. The H/P domain is highly conserved among species, and because rabbit H/P domain is more resistant to internal proteolytic cleavage than the human domain, the rabbit HPRG (rbHPRG) was primarily used to assess the antiangiogenic activity of HPRG. Rabbit HPRG **inhibited** human umbilical vein endothelial cell (HUVEC) tube formation stimulated by fibroblast growth factor-2 (FGF-2) or vascular endothelial growth factor on a Matrigel surface as well as cell proliferation of FGF-2 stimulated HUVECs. The antiangiogenic activity of rbHPRG was localized to the H/P domain by use of proteolytic fragments of rbHPRG and was further confirmed and characterized in two in vivo models of **angiogenesis**: the chorioallantoic membrane of the chick assay and the mouse Matrigel plug assay. Caspase-3 activation was observed in HUVECs stimulated with FGF-2 in the presence of rbHPRG, suggesting that apoptosis of activated endothelial cells may be one of the mechanisms underlying its antiangiogenic activity. Finally, the H/P domain of rbHPRG reduced tumor cell number when tumor cells were co-inoculated in the Matrigel plug assay. In conclusion, the H/P domain within HPRG induces the apoptosis of activated endothelial cells leading to potent antiangiogenic effects.
ACCESSION NUMBER: 2002472915 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12235005
TITLE: Histidine-proline-rich glycoprotein has potent antiangiogenic activity mediated through the histidine-proline-rich domain.
AUTHOR: Juarez Jose C; Guan Xiaojun; Shipulina Natalya V; Plunkett Marian L; Parry Graham C; Shaw David Elliot; Zhang Jing-Chuan; Rabbani Shafaat A; McCrae Keith R; Mazar Andrew P; Morgan William T; Donate Fernando
CORPORATE SOURCE: Attenuon, LLC, 10130 Sorrento Valley Road, Suite B, San Diego, CA 92121, USA.
CONTRACT NUMBER: CA 83134 (NCI)
SOURCE: Cancer research, (2002 Sep 15) 62 (18) 5344-50. Journal code: 2984705R. ISSN: 0008-5472.
PUB. COUNTRY: United States

DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020918
Last Updated on STN: 20021010
Entered Medline: 20021008

L17 ANSWER 8 OF 32 MEDLINE on STN
TI **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (**HKa**) and **kininogen**-derived polypeptides.
AB We recently reported that the two-chain form of human high molecular weight **kininogen** (**HKa**) **inhibits** **angiogenesis** by inducing endothelial cell apoptosis (Zhang et al. 2000). This property appears to be primarily conferred by **HKa** domain 5 (**HKa** D5). In this manuscript, we further characterize the activity of these polypeptides toward proliferating endothelial cells, as well as their in vivo anti-angiogenic activity in the chick chorioallantoic membrane (CAM). We also demonstrate that short peptides derived from endothelial cell binding regions in **HKa** domains 3 and 5 **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis. Like **HKa** and **HKa** D5, peptides derived from the latter domain induce endothelial cell apoptosis in a Zn(2+)-dependent manner, while those derived from domain 3 function independently of Zn2+. The implications of these findings to the regulation of **angiogenesis** and development of anti-angiogenic therapeutics are discussed.
ACCESSION NUMBER: 2002201026 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11934260
TITLE: **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (**HKa**) and **kininogen**-derived polypeptides.
AUTHOR: Zhang Jing-Chuan; Qi Xiaoping; Juarez Jose; Plunkett Marian; Donate Fernando; Sakthivel Ramasamy; Mazar Andrew P; McCrae Keith R
CORPORATE SOURCE: Department of Medicine, Case Western Reserve University, School of Medicine, University Hospitals of Cleveland, OH 44106-4937, USA.
CONTRACT NUMBER: R01 CA83134 (NCI)
SOURCE: Canadian journal of physiology and pharmacology, (2002 Feb) 80 (2) 85-90.
Journal code: 0372712. ISSN: 0008-4212.
PUB. COUNTRY: Canada
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200210
ENTRY DATE: Entered STN: 20020406
Last Updated on STN: 20021019
Entered Medline: 20021018

L17 ANSWER 9 OF 32 MEDLINE on STN
TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AB Cleavage of high molecular weight **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. **HKa** or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. **HKa** or D5 is antiadhesive by competing with vitronectin binding to the urokinase

receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001504474 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11258675
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AUTHOR: Colman R W
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA 19140, USA.
SOURCE: Biological chemistry, (2001 Jan) 382 (1) 65-70. Ref: 22
Journal code: 9700112. ISSN: 1431-6730.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
(REVIEW, TUTORIAL)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200109
ENTRY DATE: Entered STN: 20010917
Last Updated on STN: 20010917
Entered Medline: 20010913

L17 ANSWER 10 OF 32 MEDLINE on STN
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: partial activity within domain 5.
AB We previously reported that the binding of two-chain high molecular weight **kininogen** (**HKa**) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of **HKa** binding on endothelial cell proliferation. Unexpectedly, **HKa** **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by approximately 10 nM **HKa**. This activity was Zn(2+) dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. **HKa** selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by **HKa** was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or **HKa** to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of **HKa**. In vivo, **HKa** **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that **HKa** is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2001111838 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11099478
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits** **angiogenesis**: partial activity within domain 5.
AUTHOR: Zhang J C; Claffey K; Sakthivel R; Darzynkiewicz Z; Shaw D E; Leal J; Wang Y C; Lu F M; McCrae K R
CORPORATE SOURCE: Hematology-Oncology Division, Case Western Reserve University, School of Medicine, Cleveland, Ohio 44106-4937, USA.
CONTRACT NUMBER: CA83134 (NCI)
HL50827 (NHLBI)

SOURCE: FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2000 Dec) 14 (15) 2589-600.
Journal code: 8804484. ISSN: 0892-6638.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200102
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010208

L17 ANSWER 11 OF 32 MEDLINE on STN
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (**HKa**) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 microM with an IC(50) (concentration to yield 50% **inhibition**) = 0.12 microM. A D5 peptide, G486-K502, showed an IC(50) = 0.2 microM, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 microM (IC(50) > 50 microM). D6 exhibited weaker **inhibitory** activity (IC(50) = 0.50 microM). D5 also potently **inhibited** endothelial cell proliferation with an IC(50) = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC(50) = 100 nM) in **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, "kininostatin") is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo. (Blood. 2000;95:543-550)
ACCESSION NUMBER: 2000094677 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10627460
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AUTHOR: Colman R W; Jameson B A; Lin Y; Johnson D; Mousa S A
CORPORATE SOURCE: Sol Sherry Thrombosis Research Center, Temple University School of Medicine, Philadelphia, PA 19140, USA..
colmanr@astro.temple.edu
CONTRACT NUMBER: PO1HL56914 (NHLBI)
RO1CA63938 (NCI)
SOURCE: Blood, (2000 Jan 15) 95 (2) 543-50.
Journal code: 7603509. ISSN: 0006-4971.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200002
ENTRY DATE: Entered STN: 20000209
Last Updated on STN: 20000209

Entered Medline: 20000203

L17 ANSWER 12 OF 32 USPATFULL on STN
TI Histidine proline rich glycoprotein (HPRG) as an anti-angiogenic and anti-tumor agent
AB Histidine Proline Rich Glycoprotein (HPRG) polypeptides or fragments thereof including pentapeptide fragments and multimers thereof, and other biologically active derivatives of HPRG are anti-angiogenic. These compounds may be used to **inhibit angiogenesis** or treat a disease or condition in which **angiogenesis** is pathogenic. These compounds therefore have anti-tumor activity and are used in methods for **inhibiting** the growth of primary tumors or metastases. Antibodies specific for epitopes of the His-Pro rich domain of HPRG are stimulators of **angiogenesis** and are useful for promoting neovascularization in pertinent disease states.

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

ACCESSION NUMBER:	2003:120259 USPATFULL		
TITLE:	Histidine proline rich glycoprotein (HPRG) as an anti-angiogenic and anti-tumor agent		
INVENTOR(S):	Donate, Fernando, San Diego, CA, UNITED STATES Harris, Scott, San Diego, CA, UNITED STATES Plunkett, Marian L., San Diego, CA, UNITED STATES Mazar, Andrew P., San Diego, CA, UNITED STATES		
	NUMBER	KIND	DATE
PATENT INFORMATION:	US 2003082740	A1	20030501
APPLICATION INFO.:	US 2002-74225	A1	20020214 (10)
	NUMBER		DATE
PRIORITY INFORMATION:	US 2001-268370P		20010214 (60)
DOCUMENT TYPE:	Utility		
FILE SEGMENT:	APPLICATION		
LEGAL REPRESENTATIVE:	Venable, P.O. Box 34385, Washington, DC, 20043-9998		
NUMBER OF CLAIMS:	51		
EXEMPLARY CLAIM:	1		
NUMBER OF DRAWINGS:	7 Drawing Page(s)		
LINE COUNT:	3231		

CAS INDEXING IS AVAILABLE FOR THIS PATENT.

L17 ANSWER 13 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AN AAY81999 peptide DGENE
AB The present sequence is derived from human two-chain high molecular weight **kininogen** (**HKa**) domain 5. **HKa** is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. **Hka** or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**.
Angiogenesis occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.
ACCESSION NUMBER: AAY81999 peptide DGENE

TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human two-chain high molecular weight **kininogen** domain 5 fragment #8.

L17 ANSWER 14 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AN AAY81998 peptide DGENE
AB The present sequence is derived from human two-chain high molecular weight **kininogen** (**HKa**) domain 5. **HKa** is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. **Hka** or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting** **angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit** **angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.
ACCESSION NUMBER: AAY81998 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM)UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human two-chain high molecular weight **kininogen** domain 5 fragment #7.

L17 ANSWER 15 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AN AAY81997 peptide DGENE
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (**HKa**) by plasma kallikrein. **Hka** or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting** **angiogenesis**. **Angiogenesis** occurs

in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81997 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human high molecular weight **kininogen** domain 5 fragment #6.

L17 ANSWER 16 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AN AAY81996 peptide DGENE
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (**HKa**) by plasma kallikrein. **Hka** or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting** **angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit** **angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81996 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human high molecular weight **kininogen** domain 5 fragment #5.

L17 ANSWER 17 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit**

angiogenesis, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AN AAY81995 peptide DGENE

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (**HKa**) by plasma kallikrein. **Hka** or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81995 peptide DGENE

TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000027866 A1 20000518 52p

APPLICATION INFO: WO 1999-US26419 19991105

PRIORITY INFO: US 1998-107833 19981110

DOCUMENT TYPE: Patent

LANGUAGE: English

OTHER SOURCE: 2000-376483 [32]

DESCRIPTION: Human high molecular weight **kininogen** domain 5 fragment #4.

L17 ANSWER 18 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN

TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

AN AAY81994 peptide DGENE

AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (**HKa**) by plasma kallikrein. **Hka** or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81994 peptide DGENE

TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -

INVENTOR: McCrae R K

PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.

PATENT INFO: WO 2000027866 A1 20000518 52p

APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human high molecular weight **kininogen** domain 5 fragment #3.

L17 ANSWER 19 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AN AAY81993 peptide DGENE
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (**HKa**) by plasma kallikrein. **Hka** or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**.
Angiogenesis occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit** **angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.
ACCESSION NUMBER: AAY81993 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human high molecular weight **kininogen** domain 5 fragment #2.

L17 ANSWER 20 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit** **angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AN AAY81992 peptide DGENE
AB The present sequence is derived from human high molecular weight **kininogen** (HK) domain 5. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells, where it is cleaved to two-chain high molecular weight **kininogen** (**HKa**) by plasma kallikrein. **Hka** or a synthetic compound comprising part or all of the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**.
Angiogenesis occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit** **angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or

synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAY81992 peptide DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human high molecular weight **kininogen** domain 5 fragment #1.

L17 ANSWER 21 OF 32 DGENE COPYRIGHT 2004 THOMSON DERWENT on STN
TI A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
AN AAB06337 Protein DGENE
AB The present sequence is derived from human two-chain high molecular weight **kininogen** (**HKa**) domain 5. **HKa** is product of high molecular weight **kininogen** (HK) cleavage by plasma kallikrein. HK is a 120 kD glycoprotein which binds with high affinity to endothelial cells. **Hka** or a synthetic compound comprising the present sequence may be used in a pharmaceutical composition for **inhibiting angiogenesis**. **Angiogenesis** occurs in a number of disease states, such as tumour formation and expansion, and certain ocular disorders. It can also occur in a rheumatoid joint, hastening joint destruction by allowing an influx of leukocytes. The composition may **inhibit angiogenesis** by **inhibiting** endothelial cell proliferation or by inducing endothelial cell apoptosis. Peptides used in the compostion may be recombinant peptides, natural peptides, or synthetic peptides. They may also be chemically synthesised, using, for example, solid phase synthesis methods.

ACCESSION NUMBER: AAB06337 Protein DGENE
TITLE: A pharmaceutical composition used to **inhibit angiogenesis**, **inhibit** endothelial cell proliferation, and induce endothelial cell apoptosis -
INVENTOR: McCrae R K
PATENT ASSIGNEE: (UTEM) UNIV TEMPLE.
(MCCR-I) MCCRAE R K.
PATENT INFO: WO 2000027866 A1 20000518 52p
APPLICATION INFO: WO 1999-US26419 19991105
PRIORITY INFO: US 1998-107833 19981110
DOCUMENT TYPE: Patent
LANGUAGE: English
OTHER SOURCE: 2000-376483 [32]
DESCRIPTION: Human two-chain high molecular weight **kininogen** domain 5 fragment #9.

L17 ANSWER 22 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Apoptotic effect of cleaved high molecular weight **kininogen** is regulated by extracellular matrix proteins.
AB We previously reported that cleaved high molecular weight **kininogen** (**HKa**) and its domain 5 (D5) **inhibit** critical steps required for **angiogenesis** and in vivo neovascularization (Colman et al. [2000]: Blood 95:543-550). We have further shown that D5 is able to induce apoptosis of endothelial cells,

which may represent a critical part of the antiangiogenic activity of **HKa** and D5 (Guo et al. [2001]: Arterioscler Thromb Vasc Biol 21:1427-1433). In this study, we demonstrate that **HKa**- and D5-induced apoptosis is closely correlated with their anti-adhesive effect. An important new finding is that the apoptotic activity of **HKa** and D5 is highly regulated by their interactions with different extracellular matrix (ECM) proteins. H Ka **inhibited** cell adhesion to vitronectin (Vn, 90%) and gelatin (Gel) (40%), but it had no apparent effect on cell adhesion to fibronectin (Fn). D5 showed a similar pattern on cell adhesion but was less potent than **HKa**. **HKa** induced apoptosis of endothelial cells grown on Vn and Gel but not cells grown on Fn which closely parallels with its antiadhesive potency. Further results revealed that the anti-adhesive effect and the apoptotic effect of **HKa** are associated with its ability to **inhibit** phosphorylation of focal adhesion kinase (FAK) and paxillin, two important signal molecules required for cell adhesion and cell viability. We conclude that the anti-adhesive activity of **HKa** and D5 is responsible for their apoptotic effect and that Vn is likely an ECM component that mediates the effect of **HKa** and D5. .COPYRGT. 2003 Wiley-Liss, Inc.

ACCESSION NUMBER: 2003222623 EMBASE
TITLE: Apoptotic effect of cleaved high molecular weight **kininogen** is regulated by extracellular matrix proteins.
AUTHOR: Guo Y.-L.; Wang S.; Cao D.J.; Colman R.W.
CORPORATE SOURCE: Dr. Y.-L. Guo, Sol Sherry Thromb. Research Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, United States. yguo0002@astro.temple.edu
SOURCE: Journal of Cellular Biochemistry, (1 Jun 2003) 89/3 (622-632). Refs: 45 ISSN: 0730-2312 CODEN: JCEBD5
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 23 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Upregulation of Cdc2 and cyclin A during apoptosis of endothelial cells induced by cleaved high-molecular-weight **kininogen**.
AB We (8) reported that the cleaved high-molecular-weight **kininogen** (**HKa**) and its domain 5 (D5) **inhibited** **angiogenesis**. Further studies (15) revealed that D5 could **inhibit** cell proliferation and induce apoptosis of proliferating endothelial cells, which together may represent a critical part of antiangiogenic activity of **HKa** and D5. In the present study, we further examined the effect of **HKa** on cell cycle progression and cell viability. We report that **HKa** induced a significant upregulation of Cdc2 and cyclin A in proliferating endothelial cells, concurrent with a marked increase of Cdc2 activity. The increased expression of Cdc2 and cyclin A by **HKa** was not associated with an apparent change in cell cycle profiles of basic fibroblast growth factor-stimulated proliferating cells, but closely correlated with a marked increase of apoptosis, suggesting that the elevated Cdc2 activity is involved in **HKa**-induced apoptosis of proliferating endothelial cells. Our results support an emerging hypothesis that Cdc2 and cyclin A are important regulators for cell cycle as well as for apoptosis.

ACCESSION NUMBER: 2003214698 EMBASE
TITLE: Upregulation of Cdc2 and cyclin A during apoptosis of endothelial cells induced by cleaved high-molecular-weight

kininogen.

AUTHOR: Wang S.; Hasham M.G.; Isordia-Salas I.; Tsygankov A.Y.; Colman R.W.; Guo Y.-L.

CORPORATE SOURCE: Y.-L. Guo, Sol Sherry Thromb. Research Center, Temple Univ. School of Medicine, 3400 N. Broad St., Philadelphia, PA 19140, United States. yguo0002@astro.temple.edu

SOURCE: American Journal of Physiology - Heart and Circulatory Physiology, (1 Jun 2003) 284/6 53-6 (H1917-H1923).
Refs: 31
ISSN: 0363-6135 CODEN: AJPPDI

COUNTRY: United States

DOCUMENT TYPE: Journal; Article

FILE SEGMENT: 002 Physiology
029 Clinical Biochemistry

LANGUAGE: English

SUMMARY LANGUAGE: English

L17 ANSWER 24 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

TI Kininostatin as an antiangiogenic **inhibitor**: What we know and what we do not know.

AB High-molecular-weight **kininogen** (HK) is a plasma protein consisting of six domains (designated D1-D6). It was first characterized as a precursor of bradykinin, a bioactive peptide that regulates many cardiovascular processes. HK can bind to endothelial cells where it can be cleaved by plasma kallikrein to release bradykinin contained within domain 4. The remaining portion of the molecule, cleaved HK, is designated **HKa**. While bradykinin has been intensively studied, the physiological implication of the generation of **HKa** is not clear. **HKa** has recently been shown to **inhibit** the important steps required for **angiogenesis** such as proliferation and migration of endothelial cells. The antiangiogenic activity of **HKa** has further been demonstrated in animal models in which **HKa** **inhibits** neovascularization. Because domain 5 (D5) of **HKa** reproduces the antiangiogenic effect of **HKa**, D5 is named kininostatin for this novel function. In this review, we will briefly discuss the recent progress in the studies of the molecular mechanisms that mediate the antiangiogenic effect of **HKa** and D5. .COPYRGT. 2002 Elsevier Science B.V. All rights reserved.

ACCESSION NUMBER: 2002427789 EMBASE

TITLE: Kininostatin as an antiangiogenic **inhibitor**: What we know and what we do not know.

AUTHOR: Guo Y.-L.; Wang S.; Colman R.W.

CORPORATE SOURCE: Y.-L. Guo, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, United States. yguo0002@astro.temple.edu

SOURCE: International Immunopharmacology, (2002) 2/13-14 (1931-1940).
Refs: 66
ISSN: 1567-5769 CODEN: IINMBA

PUBLISHER IDENT.: S 1567-5769(02)00172-8

COUNTRY: Netherlands

DOCUMENT TYPE: Journal; General Review

FILE SEGMENT: 016 Cancer
025 Hematology
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index

LANGUAGE: English

SUMMARY LANGUAGE: English

L17 ANSWER 25 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

TI **Inhibition** of **angiogenesis** by a monoclonal antibody to **kininogen** as well as by kininostatin which block proangiogenic high molecular weight **kininogen**.

AB High molecular weight **kininogen** (HK) exhibits two activities with respect to **angiogenesis** after cleavage by plasma kallikrein. Cleaved HK (**HKa**) and its cell-binding domain 5 (D5), kininostatin, are potent antiangiogenic polypeptides. They **inhibit** endothelial cell migration, proliferation and tube formation. **HKa** and D5 **inhibit angiogenesis** in the chicken chorioallantoic membrane (CAM) assay. D5 stimulates apoptosis and interferes with the cell cycle. In contrast, intact HK is proangiogenic by liberating bradykinin. A monoclonal antibody to HK can **inhibit angiogenesis** in the CAM assay, human colon carcinoma growing as a xenograft in nude mice, and murine hybridomas growing in syngeneic hosts. Not only are the tumors decreased in volume and weight to isotype controls but the mean vascular density is decreased. Thus, both D5 and its constituent peptide and monoclonal antibody have potential for **inhibiting angiogenesis** and tumor growth in human therapy.

ACCESSION NUMBER: 2002427786 EMBASE
TITLE: **Inhibition** of **angiogenesis** by a monoclonal antibody to **kininogen** as well as by kininostatin which block proangiogenic high molecular weight **kininogen**.
AUTHOR: Colman R.W.
CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Research Ctr., Temple University School of Medicine, 3400 North Broad Street, Philadelphia, PA 19140, United States. colmanr@astro.temple.edu
SOURCE: International Immunopharmacology, (2002) 2/13-14 (1887-1894). Refs: 17 ISSN: 1567-5769 CODEN: IINMBA
PUBLISHER IDENT.: S 1567-5769(02)00173-X
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 026 Immunology, Serology and Transplantation
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 26 OF 32 EMBASE on STN

TI The antiangiogenic activity of cleaved high molecular weight **kininogen** is mediated through binding to endothelial cell tropomyosin.

AB Conformationally altered proteins and protein fragments derived from the extracellular matrix and hemostatic system may function as naturally occurring **angiogenesis inhibitors**. One example of such a protein is cleaved high molecular weight **kininogen** (**HKa**). **HKa inhibits angiogenesis** by inducing apoptosis of proliferating endothelial cells, effects mediated largely by **HKa** domain 5. However, the mechanisms underlying the antiangiogenic activity of **HKa** have not been characterized, and its binding site on proliferating endothelial cells has not been defined. Here, we report that the induction of endothelial cell apoptosis by **HKa**, as well as the antiangiogenic activity of **HKa** in the chick chorioallantoic membrane, was **inhibited** completely by antitropomyosin monoclonal antibody TM-311. TM-311 also blocked the high-affinity Zn(2+)-dependent binding of **HKa** to both purified tropomyosin and proliferating endothelial cells. Confocal microscopic analysis of endothelial cells stained with monoclonal antibody TM-311, as well as biotin labeling of cell surface proteins on intact endothelial cells, revealed that tropomyosin exposure was enhanced on the surface of

proliferating cells. These studies demonstrate that the antiangiogenic effects of **HKa** depend on high-affinity binding to endothelial cell tropomyosin.

ACCESSION NUMBER: 2002339194 EMBASE
TITLE: The antiangiogenic activity of cleaved high molecular weight **kininogen** is mediated through binding to endothelial cell tropomyosin.
AUTHOR: Zhang J.-C.; Donate F.; Qi X.; Ziats N.P.; Juarez J.C.; Mazar A.P.; Pang Y.-P.; McCrae K.R.
CORPORATE SOURCE: K.R. McCrae, Hematology-Oncology, BRB 3, Case W. Reserve Univ. Sch. of Med., 10900 Euclid Avenue, Cleveland, OH 44106-4937, United States. kxm71@po.cwru.edu
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (17 Sep 2002) 99/19 (12224-12229).
Refs: 42
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
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FILE SEGMENT: 029 Clinical Biochemistry
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 27 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Histidine-proline-rich glycoprotein has potent antiangiogenic activity mediated through the histidine-proline-rich domain.
AB Histidine-proline-rich glycoprotein (HPRG) is an abundant multi-domain plasma protein evolutionarily related to high-molecular-weight **kininogen**. The cleaved form of high-molecular-weight **kininogen** has recently been demonstrated to exhibit antiangiogenic activities in vitro (J. C. Zhang et al., FASEB J., 14: 2589-2600, 2000), mediated primarily through domain 5. HPRG contains a histidine-proline-rich (H/P) domain with sequence and functional similarities to **HKa** -D5. We hypothesized that HPRG may also have antiangiogenic properties, localized within its H/P domain. The H/P domain is highly conserved among species, and because rabbit H/P domain is more resistant to internal proteolytic cleavage than the human domain, the rabbit HPRG (rbHPRG) was primarily used to assess the antiangiogenic activity of HPRG. Rabbit HPRG **inhibited** human umbilical vein endothelial cell (HUVEC) tube formation stimulated by fibroblast growth factor-2 (FGF-2) or vascular endothelial growth factor on a Matrigel surface as well as cell proliferation of FGF-2 stimulated HUVECs. The antiangiogenic activity of rbHPRG was localized to the H/P domain by use of proteolytic fragments of rbHPRG and was further confirmed and characterized in two in vivo models of **angiogenesis**: the chorioallantoic membrane of the chick assay and the mouse Matrigel plug assay. Caspase-3 activation was observed in HUVECs stimulated with FGF-2 in the presence of rbHPRG, suggesting that apoptosis of activated endothelial cells may be one of the mechanisms underlying its antiangiogenic activity. Finally, the H/P domain of rbHPRG reduced tumor cell number when tumor cells were co-inoculated in the Matrigel plug assay. In conclusion, the H/P domain within HPRG induces the apoptosis of activated endothelial cells leading to potent antiangiogenic effects.

ACCESSION NUMBER: 2002330619 EMBASE
TITLE: Histidine-proline-rich glycoprotein has potent antiangiogenic activity mediated through the histidine-proline-rich domain.
AUTHOR: Juarez J.C.; Guan X.; Shipulina N.V.; Plunkett M.L.; Parry G.C.; Shaw D.E.; Zhang J.-C.; Rabbani S.A.; McCrae K.R.; Mazar A.P.; Morgan W.T.; Donate F.
CORPORATE SOURCE: F. Donate, Attenuon, LLC, 10130 Sorrento Valley Road, San Diego, CA 92121, United States. donate@attenuon.com

SOURCE: Cancer Research, (15 Sep 2002) 62/18 (5344-5350).
Refs: 39
ISSN: 0008-5472 CODEN: CNREA8
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 016 Cancer
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 28 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

TI **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (**HKa**) and **kininogen**-derived polypeptides.

AB We recently reported that the two-chain form of human high molecular weight **kininogen** (**HKa**) **inhibits angiogenesis** by inducing endothelial cell apoptosis (Zhang et al. 2000). This property appears to be primarily conferred by **HKa** domain 5 (**HKa** D5). In this manuscript, we further characterize the activity of these polypeptides toward proliferating endothelial cells, as well as their in vivo anti-angiogenic activity in the chick chorioallantoic membrane (CAM). We also demonstrate that short peptides derived from endothelial cell binding regions in **HKa** domains 3 and 5 **inhibit** endothelial cell proliferation and induce endothelial cell apoptosis. Like **HKa** and **HKa** D5, peptides derived from the latter domain induce endothelial cell apoptosis in a Zn(2+)-dependent manner, while those derived from domain 3 function independently of Zn(2+). The implications of these findings to the regulation of **angiogenesis** and development of anti-angiogenic therapeutics are discussed.

ACCESSION NUMBER: 2002117715 EMBASE
TITLE: **Inhibition** of **angiogenesis** by two-chain high molecular weight **kininogen** (**HKa**) and **kininogen**-derived polypeptides.
AUTHOR: Zhang J.-C.; Qi X.; Juarez J.; Plunkett M.; Donate F.; Sakthivel R.; Mazar A.P.; McCrae K.R.
CORPORATE SOURCE: K.R. McCrae, Department of Medicine, Case Western Reserve University, Sch. Med./Univ. Hosp. of Cleveland, Cleveland, OH 44106-4937, United States. kxm71@po.cwru.edu
SOURCE: Canadian Journal of Physiology and Pharmacology, (2002) 80/2 (85-90).
Refs: 19
ISSN: 0008-4212 CODEN: CJPPA3
COUNTRY: Canada
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English; French

L17 ANSWER 29 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN

TI Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.

AB Cleavage of high molecular weight **kininogen** (HK) by plasma kallikrein results in a light chain and a heavy chain (HK). The light chain has two domains: D6, which binds (pre)kallikrein, and D5, which binds to anionic surfaces, including heparin as well as zinc. Initially, HK was thought to be important for surface-activated coagulation. **HKa** or D5 binds to the urokinase receptor on endothelial cells, thereby enhancing the conversion of prourokinase to urokinase by kallikrein, and, thus, cell-associated fibrinolysis. **HKa** or D5

is antiadhesive by competing with vitronectin binding to the urokinase receptor and/or forming a complex with vitronectin. D5 **inhibits** endothelial cell migration, proliferation, tube formation and **angiogenesis**, thus modulating inflammation and neovascularization.

ACCESSION NUMBER: 2001080473 EMBASE
TITLE: Role of the light chain of high molecular weight **kininogen** in adhesion, cell-associated proteolysis and **angiogenesis**.
AUTHOR: Colman R.W.
CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Research Ctr., Temple University School of Medicine, Philadelphia, PA 19140, United States
SOURCE: Biological Chemistry, (2001) 382/1 (65-70).
Refs: 22
ISSN: 1431-6730 CODEN: BICHF3
COUNTRY: Germany
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 30 OF 32 EMBASE
on STN
TI Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits angiogenesis**: Partial activity within domain 5.
AB We previously reported that the binding of two-chain high molecular weight **kininogen** (**HKa**) to endothelial cells may occur through interactions with endothelial urokinase receptors. Since the binding of urokinase to urokinase receptors activates signaling responses and may stimulate mitogenesis, we assessed the effect of **HKa** binding on endothelial cell proliferation. Unexpectedly, **HKa** **inhibited** proliferation in response to several growth factors, with 50% **inhibition** caused by .apprx.10 nM **HKa**. This activity was Zn2+ dependent and not shared by either single-chain high molecular weight **kininogen** (HK) or low molecular weight **kininogen**. **HKa** selectively **inhibited** the proliferation of human umbilical vein and dermal microvascular endothelial cells, but did not affect that of umbilical vein or human aortic smooth muscle cells, trophoblasts, fibroblasts, or carcinoma cells. **Inhibition** of endothelial proliferation by **HKa** was associated with endothelial cell apoptosis and unaffected by antibodies that block the binding of HK or **HKa** to any of their known endothelial receptors. Recombinant HK domain 5 displayed activity similar to that of **HKa**. In vivo, **HKa** **inhibited** neovascularization of subcutaneously implanted Matrigel plugs, as well as rat corneal **angiogenesis**. These results demonstrate that **HKa** is a novel **inhibitor** of **angiogenesis**, whose activity is dependent on the unique conformation of the two-chain molecule.

ACCESSION NUMBER: 2000436640 EMBASE
TITLE: Two-chain high molecular weight **kininogen** induces endothelial cell apoptosis and **inhibits** **angiogenesis**: Partial activity within domain 5.
AUTHOR: Zhang J.-C.; Claffey K.; Sakthivel R.; Darzynkiewicz Z.; Shaw D.E.; Leal J.; Wang Y.-C.; Lu F.-M.; McCrae K.R.
CORPORATE SOURCE: K.R. McCrae, Hematology-Oncology Division, Case Western Reserve University, School of Medicine, 10900 Euclid Ave., Cleveland, OH 44106-4937, United States. kxm71@po.cwru.edu
SOURCE: FASEB Journal, (2000) 14/15 (2589-2600).
Refs: 69
ISSN: 0892-6638 CODEN: FAJOEC
COUNTRY: United States

DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 31 OF 32 EMBASE COPYRIGHT 2004 ELSEVIER INC. ALL RIGHTS RESERVED. on STN
TI Domain 5 of high molecular weight **kininogen** (kininostatin) down-regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AB We have demonstrated that high molecular weight **kininogen** (HK) binds specifically on endothelial cells to domain 2/3 of the urokinase receptor (uPAR). **Inhibition** by vitronectin suggests that kallikrein-cleaved HK (**HKa**) is antiadhesive. Plasma kallikrein bound to HK cleaves prourokinase to urokinase, initiating cell-associated fibrinolysis. We postulated that HK cell binding domains would **inhibit angiogenesis**. We found that recombinant domain 5 (D5) **inhibited** endothelial cell migration toward vitronectin 85% at 0.27 μM with an IC50 (concentration to yield 50% **inhibition**) =0.12 μM. A D5 peptide, G486-K502, showed an IC50 = 0.2 μM, but a 25-mer peptide from a D3 cell binding domain only **inhibited** migration 10% at 139 μM (IC50 > 50 μM). D6 exhibited weaker **inhibitory** activity (IC50 = 0.50 μM). D5 also potently **inhibited** endothelial cell proliferation with an IC50 = 30 nM, while D3 and D6 were inactive. Using deletion mutants of D5, we localized the smallest region for full activity to H441-D474. To further map the active region, we created a molecular homology model of D5 and designed a series of peptides displaying surface loops. Peptide 440-455 was the most potent (IC50 = 100 nM) In **inhibiting** proliferation but did not **inhibit** migration. D5 **inhibited angiogenesis** stimulated by fibroblast growth factor FGF2 (97%) in a chicken chorioallantoic membrane assay at 270 nM, and peptide 400-455 was also **inhibitory** (79%). HK D5 (for which we suggest the designation, 'kininostatin') is a potent **inhibitor** of endothelial cell migration and proliferation in vitro and of **angiogenesis** in vivo.
ACCESSION NUMBER: 2000028682 EMBASE
TITLE: Domain 5 of high molecular weight **kininogen** (kininostatin) down- regulates endothelial cell proliferation and migration and **inhibits angiogenesis**.
AUTHOR: Colman R.W.; Jameson B.A.; Lin Y.; Johnson D.; Mousa S.A.
CORPORATE SOURCE: R.W. Colman, Sol Sherry Thrombosis Res. Center, Temple University School of Medicine, 3400 North Broad St, Philadelphia, PA 19140, United States. colmanr@astro.temple.edu
SOURCE: Blood, (15 Jan 2000) 95/2 (543-550).
Refs: 52
ISSN: 0006-4971 CODEN: BLOOAW
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 025 Hematology
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English

L17 ANSWER 32 OF 32 WPIDS COPYRIGHT 2004 THOMSON DERWENT on STN
TI New tropomyosin-related antiangiogenic receptor polypeptide, useful for **inhibiting** endothelial cell migration, invasion, proliferation or **angiogenesis**, inducing endothelial cell apoptosis, or treating tumors or cancer.
AN 2004-090604 [09] WPIDS
AB WO2003077872 A UPAB: 20040205
NOVELTY - An isolated tropomyosin-related antiangiogenic receptor

polypeptide or peptide, is new.

DETAILED DESCRIPTION - The tropomyosin (Tpm)-related antiangiogenic receptor polypeptide or peptide:

(a) is a fragment of a full-length native Tpm protein expressed on the surface of endothelial cells, or a variant of the fragment;

(b) has a molecular mass of about 17 kDa and corresponds in its sequence to, or is a variant of, an internal fragment of a native Tpm isoform which is a binding site for antiangiogenic polypeptide agents; and

(c) binds to the antiangiogenic polypeptide agents which bind to the native Tpm internal fragment binding site.

The peptide has about 4-40 amino acids, and the variant of the polypeptide or peptide is a conservative substitution variant of a native Tpm sequence. The isolated antiangiogenic receptor polypeptide, peptide or variant has substantially the same biochemical activity of binding to the antiangiogenic polypeptide agents, as does the native Tpm internal fragment.

INDEPENDENT CLAIMS are included for the following:

(1) an antibody or its antigen-binding fragment (ABF), i.e. an antiangiogenic or a proangiogenic antibody or ABF, which is specific for an epitope of a Tpm isoform expressed on the surface of an activated endothelial cell, where the antibody or ABF has: (a) antiangiogenic activity in that it binds to the activated endothelial cell, causing the generation of an antiangiogenic signal in said cell, resulting in **inhibition** of migration, invasion, proliferation or **angiogenesis**, or apoptosis; or (b) proangiogenic activity in that it binds to Tpm on the endothelial cell and **inhibits** the binding to the cell of a Tpm-binding antiangiogenic agent, permitting or promoting migration, invasion, proliferation or **angiogenesis** that would otherwise be **inhibited** by the antiangiogenic agent;

(2) an antibody useful for detecting a Tpm polypeptide or peptide that serves as an antiangiogenic receptor on endothelial cells, comprising the antibody or ABF of (1), which is detectably labeled with a detectable label;

(3) a diagnostically useful Tpm-binding antibody composition comprising the detectably labeled antibody or ABF of (2), and a diagnostic carrier;

(4) a therapeutically useful antiangiogenic or proangiogenic antibody or ABF that targets Tpm or its epitope and **inhibits** or stimulates, respectively, **angiogenesis** in vitro or in vivo, comprising the antibody or ABF of (1) to which is optionally bound, directly or indirectly, a therapeutic group;

(5) a therapeutic antiangiogenic or proangiogenic pharmaceutical composition that **inhibits** or stimulates **angiogenesis** in vitro or in vivo, comprising the antibody or ABF of (4), and a pharmaceutical carrier;

(6) a cyclic peptide about 4-20 amino acids which binds to the D5 domain of **HKa** and **inhibit angiogenesis** in an in vitro or in vivo assay of **angiogenesis**;

(7) a method for **inhibiting** endothelial cell migration, invasion, proliferation or **angiogenesis**, or for inducing endothelial cell apoptosis;

(8) a method for treating a subject having a disease or condition associated with undesired cell migration, invasion, proliferation, or **angiogenesis**;

(9) a method for stimulating **angiogenesis** in a subject;

(10) methods for detecting in a biological sample the presence of Tpm or Tpm of an isoform expressed on the surface of activated endothelial cells;

(11) a screening test to identify a test compound as a candidate antiangiogenic molecule that binds to Tpm;

(12) an affinity ligand for binding to or isolating a Tpm-binding antiangiogenic molecule or cells expressing the binding molecule, comprising the isolated polypeptide or peptide cited above, immobilized to a solid support or carrier; and

(13) a method for isolating a Tpm-binding antiangiogenic molecule from a complex mixture.

ACTIVITY - Cytostatic; Antidiabetic; Ophthalmological; Antiinflammatory; Gynecological; Antiarthritic; Antipsoriatic; Dermatological; Cardiant; Vasotropic; Vulnerary.

MECHANISM OF ACTION - **Angiogenesis Inhibitor**; **Angiogenesis** Stimulator; Gene Therapy.

Matrigel (RTM) (0.5 ml) containing 400 ng/ml of bFGF, 50 micro g/ml heparin with or without 10 micro M peptide (ATN-310, ATN-311 or ATN-312, or saline buffer as control) was injected subcutaneously in the hind flanks of a mouse. After 5 days, the vascularization of the Matrigel (RTM) plug was determined fluorometrically after intravenous injection of 100 micro l of dextran conjugated with fluorescein isothiocyanate. Results showed that all three peptides were very effective **inhibitors** of **angiogenesis**, i.e. 87.8% **inhibition** for ATN-310, 87.7% **inhibition** for ATN-311, and 81.7% **inhibition** for ATN-312.

USE - The tropomyosin (Tpm)-related antiangiogenic receptor polypeptide or peptide, antibodies and compositions are useful for **inhibiting** endothelial cell migration, invasion, proliferation or **angiogenesis**, for inducing endothelial cell apoptosis, or for treating tumors or cancer, diabetic retinopathy, neovascular glaucoma, uveitis, endometriosis, arthritis, psoriasis, or scleroderma. The antibody may be also used for detecting the presence of a Tpm polypeptide or peptide in a biological sample, for promoting wound healing, or for treating diseases or conditions in which increased **angiogenesis** is desired, e.g. coronary artery disease or peripheral artery disease.

Dwg.0/21

ACCESSION NUMBER: 2004-090604 [09] WPIDS
DOC. NO. CPI: C2004-036736
TITLE: New tropomyosin-related antiangiogenic receptor polypeptide, useful for **inhibiting** endothelial cell migration, invasion, proliferation or **angiogenesis**, inducing endothelial cell apoptosis, or treating tumors or cancer.
DERWENT CLASS: B04 D16
INVENTOR(S): DONATE, F; JUAREZ, J; MAZAR, A P; MCCRAE, K
PATENT ASSIGNEE(S): (ATTE-N) ATTENUON LLC
COUNTRY COUNT: 102
PATENT INFORMATION:

PATENT NO	KIND	DATE	WEEK	LA	PG
WO 2003077872	A2	20030925	(200409)*	EN	117

RW: AT BE BG CH CY CZ DE DK EA EE ES FI FR GB GH GM GR HU IE IT KE LS LU MC MW MZ NL OA PT RO SD SE SI SK SL SZ TR TZ UG ZM ZW

W: AE AG AL AM AT AU AZ BA BB BG BR BY BZ CA CH CN CO CR CU CZ DE DK DM DZ EC EE ES FI GB GD GE GH GM HR HU ID IL IN IS JP KE KG KP KR KZ LC LK LR LS LT LU LV MA MD MG MK MN MW MX MZ NO NZ OM PH PL PT RO RU SC SD SE SG SK SL TJ TM TN TR TT TZ UA UG US UZ VC VN YU ZA ZM ZW

APPLICATION DETAILS:

PATENT NO	KIND	APPLICATION	DATE
WO 2003077872	A2	WO 2003-US8060	20030317

PRIORITY APPLN. INFO: US 2002-364047P 20020315